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1820 "A CENTURY OF SERVICE" 1921

THE

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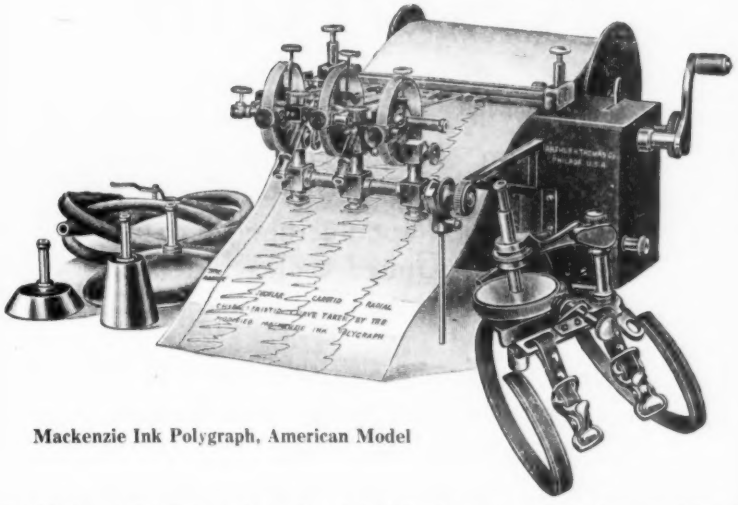

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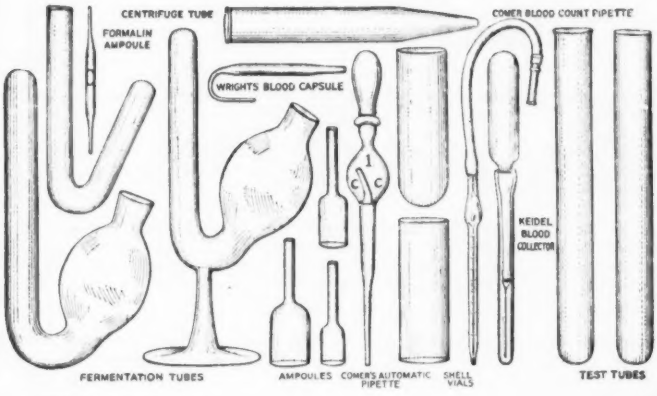

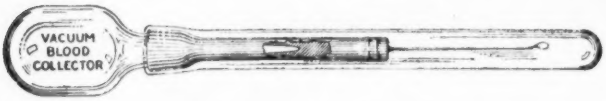

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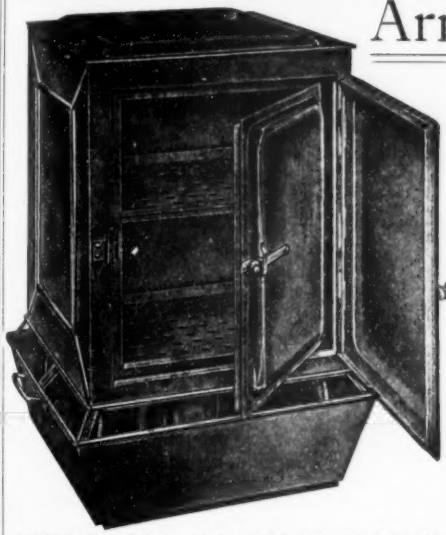

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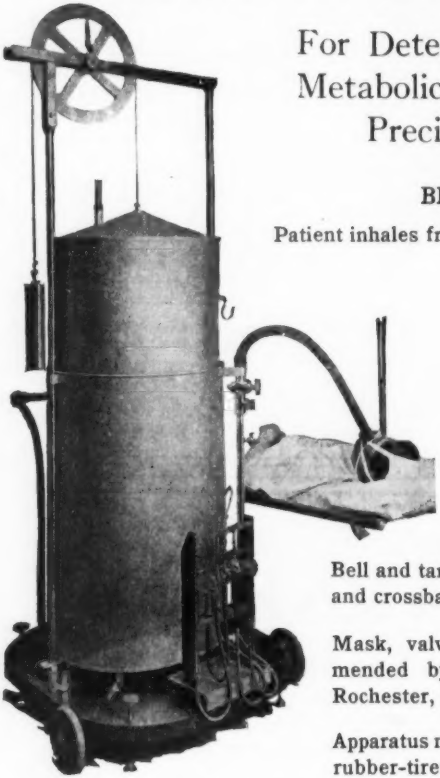

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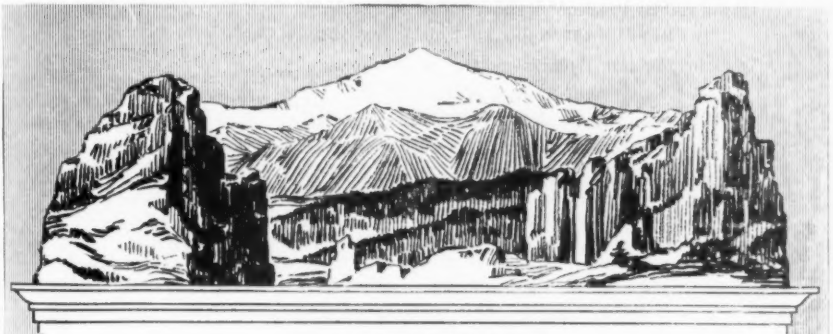

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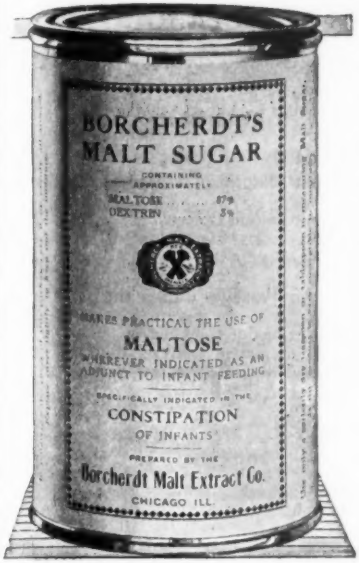

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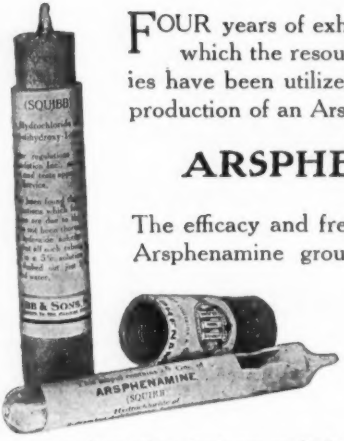

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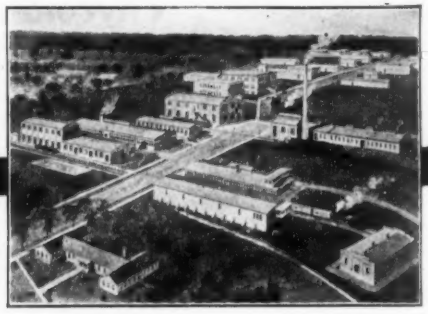

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ORIGINAL ARTICLES.

ACUTE ARTERITIS COMPLICATING PNEUMONIA.

By George Douglas Head, M.D.,

MINNEAPOLIS, MINN.

Microörganisms may enter the arterial wall either directly into the intima from the blood stream, or into the media and adventitia by way of the vasa vasorum, or through lymphatic channels, or by leukocyte carriers from diseased tissue in close proximity to the artery itself. We know the organisms are there because they have been isolated from the vessel walls in typhoid fever, diphtheria, septicemia, pneumonia, tuberculosis, syphilis and gonorrhea. When such an accident occurs in the course of an acute infection, acute inflammation of the artery may result. If the vessel is completely occluded by the thrombus, gangrene of an extremity may occur. Such cases have been observed and reported in smallpox, rheumatic fever, influenza, gonorrhea and cerebrospinal meningitis. In so widespread and common a disease as lobar pneumonia the occurrence of acute arteritis with thrombosis and gangrene should be encountered with some degree of frequency. An examination of the reported cases proves, however, the rarity of this complication.

Douillet's case is a true instance of such a complication, as is probably the case reported by Fussell, and that by Brouardel and Giroux. Abstracts of these three cases are as follows:

Douillet's case.[1]

[1] Arch. de Méd. et de Pharm. Militaire, September, 1901; Abstracted, Am. Jour. Med. Sc., 1902, cxxiii, 538.

Male, aged twenty-one years, who on the second day of defervescence from a mild pneumonia of the right lung began to complain of much pain in the left leg, which was soon followed by gangrene, and the leg was amputated at the point of election. The patient recovered. After amputation the dissection of the leg showed complete obliteration of the posterior tibial artery, the anterior tibial and the peroneal being unaltered. The obliteration was not due to an embolus but was the result of an arterial thrombosis. No bacteriologic or microscopic examination of the arterial walls was made. The patient's circulation was extremely poor during the pneumonia and during convalescence.

Fussell's case.[2]

Male, aged forty-one years, an alcoholic. Seen November 5, 1906, with a temperature of 103°, pulse 120, respirations 48 and complete consolidation of the right lung. Resolution occurred and the temperature was normal on November 8. On November 11 the man developed edema of both hands and cyanosis of the fingers of both hands. There was no cyanosis of the lips. There was also cyanosis of the lower half of both forearms, with petechiæ along the lines of the superficial veins. The afternoon of the same day the fingers became black and almost gangrenous. On November 12 the fingers of both hands were black, cold and shrivelled at the first joint. The gangrene advanced, death occurring on November 13. The postmortem revealed a bluish-black discoloration from the forearm downward. The tips of the fingers were black, shrivelled and dry. A thrombus filled the interossei arteries to a distance one inch proximal to the digital division and completely filling the digital branches. Apparently the thrombosis began in the terminal branches and spread upward.

M. G. Brouardel and M. R. Geroux,[3] relate a case of acute arteritis of the humeral artery, following pneumonia without gangrene, as follows: In 1911 Madame H., aged fifty-eight years, was seized with a violent chill and pain in the right chest, and a diagnosis of frank acute pneumonia of the lower lobe of the right lung was made. On the seventh day she complained of pain in the right shoulder and arm, with increased temperature and chills. Palpation of the humeral artery caused increased pain. Pulsation in the radial artery became lost and the limb became white and pale. No cardiac findings of an abnormal nature. No complete arrest of circulation but simple ischemia of the arm. The author concludes there was complete obliteration of the humeral artery by thrombosis, but circulation was maintained by collateral circulation because there was no thrombosis in the branches.

The large number of cases of pneumonia occurring in the army camps during the winter of 1918 and 1919 offered a splendid oppor-

[2] Am. Jour. Med. Sc., 1909, cxxxvii, 70.
[3] Société Méd. de Hôpitaux, 1913, xxxv, 1268.

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tunity for observing some of the rare complications of pneumonia. In our large experience at the Base Hospital, Camp Wheeler, Macon, Ga., one proved instance of acute arteritis with gangrene was observed (Case I). A second case (Case II) with localized gangrene of the skin of the toes was probably of like origin, and the reports of the cases are as follows:

CASE I.—*A case of lobar pneumonia complicated by arteritis and thrombosis of the right femoral and popliteal arteries. Gangrene of the leg; amputation and recovery.*

Sam. B., colored, aged twenty-three years; soldier; of good habits. Admitted to Base Hospital, Camp Wheeler, Macon, Ga., November 1, 1918. Complained of headache, nausea, vomiting and cough with fever.

CASE I.—Lobar pneumonia complicated by acute arteritis and thrombosis of the right femoral and popliteal arteries; gangrene of foot and lower third of leg; amputation; recovery. Sam. B., aged twenty-three years; soldier. Base Hospital, Camp Wheeler.[4]

Family History. Negative. The man had syphilis in 1916 and influenza in 1917. On the day of admission, the patient was taken with a chill, headache, pain in the chest on cough or deep breathing and fever (100.8°). The physical examination was negative for organic disease except the presence of a few fine crackling rales with slightly impaired percussion note in the lower right lung posteriorly.

[4] Photograph published through the courtesy of Dr. Warren Sisson, of Boston, Mass.

The diagnosis of influenza with possible lobar pneumonia (right lower lobe) was made. The second day after admission the patient's temperature was 104°, pulse 110, respirations 30. The physical examination was negative for organic disease except for an impaired percussion note at the bases of both lungs posteriorly, more marked on the right, where increased bronchophony and bronchovesicular breathing were present. The clinical diagnosis of lobar pneumonia in the right lower lobe was made by the ward surgeon and confirmed by the chief of the service. The patient had his crisis upon November 5, and on November 8 the clinical note stated that the right lobe was clearing but moist rales were still present at the base. On this date, eight days after his admission, the patient began complaining of a severe pain in the right lower leg and knee. This came on rather suddenly without apparent cause. Slight swelling was present and the tenderness was extreme from the knee downward, especially in the calf of the leg. There was no discoloration of the skin, but the leg was cold. On November 14 the patient still complained of extreme pain in the right leg. The skin of the leg looked white, wrinkled and pinched. There was slight swelling in the right foot and a mottled appearance of the leg from just above the ankle downward. A total absence of pulsation in the right dorsalis pedis was noted and the right popliteal artery showed only slight and feeble pulsation. A diagnosis of acute arteritis or embolism with thrombosis of the popliteal and anterior tibial arteries was made.

On November 29 the note of the condition of the right leg read as follows: "A line of demarcation is clearly defined on the inner aspect of the limb 10 cm. above the internal malleolus. The foot and ankle are almost completely mummified and black up to this point. There are small areas suggesting moist gangrene over the foot. There is also some swelling of soft parts in the calf of the leg. There is slight increase of temperature. The tissues of the leg are hard and indurated. No marked tenderness is present although the patient complains of extreme pain in the right leg. This, however, is not constant. There is no pulsation in the popliteal or anterior tibial arteries. The arteries of the left foot, leg and groin show normal pulsation. The pulsation in the iliac arteries can be palpated on both sides; physical signs in the lungs are clear. The heart is normal."

Urine Examination. Negative.

Blood Examination. Leukocytes, 14,800. Hemoglobin, 80 per cent. Differential count: Polynuclears, 88 per cent.; small mononuclears, 8 per cent.; large mononuclears, 3 per cent.; transitionals, 1 per cent.

Nose and throat cultures were positive for Streptococcus hemolyticus. The sputum showed a Type IV pneumococcus. Wassermann reaction positive. Inasmuch as a line of demarcation and

gangrene was established the patient was referred to the surgical side for amputation of the leg. The leg was amputated above the knee December 2. After amputation a large clot was noted plugging the cut lumen of the femoral artery. After this was removed the vessel bled freely and had to be ligated. The patient made a slow and complete recovery. A pathological study of the bloodvessel submitted for examination was reported as follows (Earl Gilroy): "There are multiple round cells in the adventitia of the femoral artery. There is slight endarteritis in the media. The interna of vessel is thick and there is a laminated collection of blood elements extending three-fourths across the lumen of the vessel."

Pathological Diagnosis: Arteritis of femoral artery with thrombosis of this artery and the popliteal artery of the right leg.

CASE II.—*A case of localized gangrene of the skin of the toes complicating bronchopneumonia.*

Hazelton, Arthur C., aged twenty-six years; white; single; soldier. Admitted to the Base Hospital, Camp Wheeler, October 28, 1918, complaining of headache, pains in the chest, cough and fever. His family history was negative. He had had measles, mumps, scarlet fever and chicken-pox. Denied venereal disease. No history of dead fingers or chilblains. One day prior to admission, while doing his work in the development battalion, the patient was taken with cold in the head and cough and pains in the back and legs. He had no distinct chill. The patient was admitted to the hospital with a temperature of 102°, pulse 88, respirations 28 and the physical signs of bronchopneumonia in the bases of both lungs. The clinical diagnosis of bronchopneumonia, bilateral, was made. The patient was very sick in the hospital from October 28 to November 4, 1918, when his temperature began dropping and the pneumonic process began gradually to resolve. On November 1, 100 c.c. of antipneumococcic serum was given. The patient showed no anaphylactic reaction following the giving of the serum or during the convalescence. On November 25, one month subsequent to entering the hospital, the patient began complaining of considerable pain on the dorsal surfaces of the third, fourth and fifth toes of the left foot. A few raised, blister-like patches appeared over the corresponding toes on the right foot, but not as marked as on the left. The appearance of the toes suggested Raynaud's disease. During November 29 and 30 the patient complained of considerable pain and a good deal of oozing from blistered-like areas on the toes. The color began to change and the toes took on a bluish, dark color and localized areas of necrosis, while ulceration appeared in the skin of the toes over the area where the blisters had first appeared. By December 4 the skin began peeling off and the ulceration areas began filling in. The patient still complained, however, of some pain in the toes. The color of the toes was now a light, greenish

color. By December 8 the skin on the toes had entirely cleared up and, aside from slight discoloration, the skin appeared healed, but the nail on the fourth toe of the left foot began to show evidence of necrosis, and on the twelfth this nail came off. Repeated careful physical examinations of this man during this interval of time showed no evidence of disease of the heart. He complained from time to time of numbness in the left thigh, some headache and general nervousness, but had no fever. The urine examination showed specific gravity, 1022; no albumin; no sugar; few granular casts.

Blood Examination. Leukocyte count, 8400; polynuclears, 54 per cent.; small mononuclears, 35 per cent.; large mononuclears, 8 per cent.; transitionals, 2 per cent. Sputum examination showed a Type IV pneumococcus. The Wassermann reaction was negative. The blood culture November 25 was negative. The patient was treated symptomatically during his sickness. At various times he was given digitalis, nux vomica and atropin (small doses). No ergot or adrenalin was given at any time. It did not seem reasonable to attribute the skin necrosis to the medication given. The diagnosis settled upon was bronchopneumonia, bilateral, complicated by gangrene of the skin of the toes of the left foot.

PERIARTERITIS NODOSA.

By Morris Manges, M.D.,

physician to mount sinai hospital; professor of clinical medicine, new york university,

and

George Baehr, M.D.,

adjunct physician and associate in pathology to mount sinai hospital.

(From the Second Medical Division and the Pathological Laboratory of Mount Sinai Hospital.)

The rare diseases have, as a rule, a clean-cut, clinical picture which enables one to recognize them readily. Periarteritis nodosa, however, is most bizarre in its manifestations, and the fact that the disease at its onset or during its course in not a few instances resembles that of an acute surgical abdominal condition makes it of interest to both internists and surgeons.

It is not our intention to present a full historical, clinical and pathological study of periarteritis nodosa, since this has already been so well done in a number of monographs. Dickson[1] brings the

[1] Jour. Pathol. and Bacteriol., 1908, xii, 31.

subject down to 1907; Longcope[2] to 1908, Lamb[3] has given the most complete discussion of this subject and has brought the literature down to 1914. Since then the most valuable contribution has been that of Klotz.[4] The most recent is that of Spiro,[5] which has appeared since this report was begun. Including our own case, the number of definitely proved cases is only 42. About a dozen or more additional cases have been properly eliminated because they do not definitely belong to this group.

As to the rarity of this disease, Schroetter[6] has given testimony when he regretfully admits that he never encountered a case of it in spite of being constantly on the watch for it in the enormous material which came under his observation in Vienna and elsewhere. While it is true that the fully developed disease is so rare, yet, as will be referred to later on, it is probable that rudimentary lesions of this type may be by no means so infrequent an occurrence, as stated by Klotz and Spiro.

The case which we shall report here is unique even for this rare disease, since it is one of the few in which the diagnosis was made during life. This has been done in four other cases, in only one of which has the diagnosis been verified by autopsy. As, fortunately, the diagnosis of our case was made early in the course of the disease, we had the unusual opportunity of studying the vascular lesions both in the early inflammatory stages as well as in the stage of healing toward which it had progressed when death occurred from the secondary nephritis. By being thus able to follow the different stages of the process and to compare them with the findings of the autopsy we have been able to correlate the varying pathological and clinical pictures described in the previously reported cases.

W. S., aged thirty-nine years, was admitted to Mount Sinai Hospital on June 6, 1919. His previous history was that he had had measles and typhus fever in childhood. As an adult his only complaint was recurrent attacks of peritonsillar abscess. His venereal history was negative.

Present History. Seven weeks before admission he had severe, cramp-like pains in the left calf which radiated into the foot. Within a few days he had similar pains in the right leg. One week later, while these were subsiding, he had severe pains in the right lumbar region which radiated into the testis. In a few days he had similar pains in the left lumbar region. Six days before admission he had bad pains in the epigastrium which did not radiate and were accompanied with marked distention and a fever of 102°. The pains and the fever have persisted. During one of the attacks of lumbar pain he passed bloody urine.

[2] Bulletin Ayer Laboratory, Pennsylvania Hospital, 1908, v, 1.
[3] Arch. Int. Med., 1914, xiv, 481.
[4] Jour. Med. Research, 1917, new series, xxxii, 1.
[5] Virchow's Arch., 1919, ccxxvii, 1.
[6] Nothnagel's specielle Pathol. und Therap., 1901, xv, ii Theil, 31.

When he was admitted to the hospital he was apparently suffering from an acute abdominal condition and he was sent to the surgical service of Dr. Edwin Beer. Shortly after his admission he was seen by Dr. L. Buerger, who, thinking that he had to deal with some lesion in the upper urinary tract, cystoscoped him and catherized the ureters. No ureteral obstruction was found. The urine was negative except for a few epithelial and red blood cells. The urea of the right kidney urine was 0.9 per cent.; that of the left kidney was 1.3 per cent.

On the next morning, when he was first seen by Dr. Beer, the patient was cheerful and felt perfectly well; in fact, when he was taken to the roentgen-ray department he asked whether he could not go home that day. It is worth noting that this curious condition of being well in the morning and being very miserable in the afternoon continued until the time of the operation. The examination showed nothing more than a vague epigastric tenderness and diseased tonsils, with a marked pharyngitis. He complained of no pain, and yet there was a very high leukocyte count of 36,000, with 75 per cent. polynuclear cells and a fever of 102°! For the following week the same condition continued. For four days he had an intermittent fever of 102° to 103°, when it suddenly dropped to normal and remained so for several weeks. The pulse and respiration ran parallel to the fever. The leukocyte count continued very high, ranging between 36,000 to 54,000, with the polynuclear cells from 76 to 90 per cent. At the end of the first week Dr. Beer could elicit some tenderness in the right hypochondrium on jarring the patient. Later on, in the same way, he found some tenderness higher up in the same area and also in the splenic region. Save for these few signs repeated examinations were negative.

The other clinical data were the following. The blood-pressure was 160/90. The blood Wassermann was negative. The chemical examination of the blood showed 35 mg. urea nitrogen; 95 mg. incoagulable nitrogen; 2 mg. creatinin; 0.136 cholesterin per 100 c.c. blood. The urine was negative save for a few red blood cells. The phenolsulphonephthalein test gave an excretion of 64 per cent. in two hours. The white cell counts and the results of the catheterization of the ureters have already been given. The blood culture was negative. From the smears of the throat a pure culture of hemolytic streptococci was obtained.

Roentgen-ray examinations of the chest, gastro-intestinal tract and kidneys were all negative. Examinations of the gastric and duodenal contents were also normal.

Gradually Dr. Beer came to the conclusion that there might be some suppurative process in the retroperitoneal glands behind the lesser omental bursa or perhaps a localized peritonitis in the lesser sac. An exploratory laparotomy, which was performed by Dr. Buerger on June 19, revealed periarteritic nodules in the mesentery,

a finding which at once cleared up many of the points in the history which had been so obscure.

All the arteries in the mesentery and in the pancreatic region were involved. Each vessel had one or more small nodular swellings, about the size of a pea, which involved the vessel uniformly like small aneurysmal enlargements. Similar nodules were found in the mesentery and in the intestinal walls. The head of the pancreas was enlarged. There was also a large solid area of fat necrosis in the omentum. The nodules were at once recognized as those of periarteritis nodosa, a diagnosis which was confirmed by the pathological examination which was made by Dr. F. S. Mandlebaum of one of the nodules excised for this purpose. The cultures from the nodule were sterile.

Five days after the operation he passed bloody urine, but this time there were no colicky pains. Two weeks later, shortly after his transfer to the Second Medical Division, he had very severe pains in both arms, the right being especially sore. This led to the finding of the first external nodules, which were felt as definite small nodes along the course of the right brachial artery. They were the size of a small pea, each of which had a small area of inflammatory reaction about it. Eleven days later (July 15) similar nodules appeared along the course of the left brachial artery and two were also found on the face, one in each anterofrontal region. The latter were the first in which there was distinct pulsation and had no inflammatory reaction. Within the following week a few not tender and uninflamed nodules appeared on each shin and also along the course of the third right intercostal artery. One of the latter was excised for pathological examination, the report of which will be found later on. Four days later two fresh nodules were found on the right side of the neck and one on the left side. Pulsation could only be detected in the nodules which had appeared on the face. At this time he also had a diffuse maculopapular rash on the hands and forearms.

He remained in the hospital for two months after the operation and he left it at his own request considerably improved; his general condition was better, although he still ran a low, irregular fever. His leukocyte count was also lower, ranging around 20,000. The pains also became much less and there were no further crops of nodules. The only new symptom was failing vision, which was due to a fibrinous exudation on the temporal side of the optic nerve heads; this was associated with a low grade of nephritis, which had been present for some weeks.

On September 3, 1919, he was readmitted to the hospital, He stated that he had been quite well for a fortnight, when he again felt sick. He had lost much weight and his chief complaints were weakness and marked dyspnea. The physical examination showed an advanced nephritis, with generalized edema. There were also

irregular patches of consolidation scattered through both lungs. Both ventricles of the heart were considerably enlarged. The liver reached to the umbilicus; the spleen could not be felt. There was a marked neuroretinitis. The urine showed an advanced nephritis. There was no fever on admission or subsequently. No glands could be felt anywhere.

The only nodules which could be found were several small hard nodules along the right temporal and brachial arteries. All the other nodules had disappeared. It is to be noted that no other nodules developed during the rest of his life.

The leukocyte count was 12,000, with 80 per cent. polynuclears, 19 per cent. small lymphocytes and 1 per cent. eosinophils. The blood-Wassermann test was again negative. The blood-chemical examination showed urea nitrogen, 49 mg. incoagulable nitrogen, 100 mg. per 100 c.c. blood. The blood-pressure was 140/100. The sputum was pneumonic in character and amounted to 30 to 60 c.c. daily. It contained streptococci and pneumococci, but no tubercle bacilli.

The most interesting findings were those in the lungs, which were naturally interpreted as being associated with vascular changes of the periarteritis nodosa in branches of the pulmonary artery. It was thought that they might be due to hemorrhages and consolidation about the aneurysmal dilatations or hemorrhagic infarcts. No information on this point could be gained from the roentgen-ray examination, which only showed dense shadows from the bases up to about the second rib. These shadows suggested pneumonia or tumor.

The electrocardiograms showed inverted *T* waves in all the leads, but were otherwise normal.

The terminal stages were those of a chronic bronchopneumonia and advanced nephritis. Death occurred on October 8, 1919.

Autopsy Report. *General.* The body is that of a rather emaciated man of large frame. No icterus or petechiæ. Moderate postmortem discoloration of the back. On the forehead, about one inch above the outer end of the left eyebrow, is a small nodule about the size of a split pea, which is apparently along the course of the temporal arteries. It is elastic in consistency. Irregular thickenings can be felt along the course of both brachial arteries.

Heart. Of normal size. The coronary vessels show a thickening of the walls, though no calcification and no distinct atherosclerotic patches. In addition, many of the descending branches of both arteries show irregular thickenings along their course. At the very apex, lying just beneath the visceral pericardium, are two nodes, pea size and apparently springing from terminal branches of the descending ramus of the left coronary. These are solid, semielastic in consistency. One consists of a sac which is filled with old blood clot, the second appears to be filled with a thrombus which

has been almost completely organized and converted into dense fibrous tissue.

Lungs. Both upper and the left lower lobes appear to be diffusely involved by a subacute lobular pneumonia; their cut section is pinkish gray in color and in places is very friable. The pleura at both apices is densely adherent. The lower lobes of both lungs and the intervening patches, between the areas of lobular pneumonia appear to be in a state of chronic edema. The tracheobronchial lymph nodes are moderately enlarged and markedly anthracotic.

Liver. Of normal size. Surface smooth; on section there appears to be a uniform thickening of the walls of the hepatic arteries. The cut ends of these vessels in Glisson's capsule stand up prominently above the cut section.

Gall-bladder and Bile Passages. Appear to be normal.

Spleen. Weight, 120 gm. About one-half normal size. Outer aspect is densely adherent to the diaphragm and anterior abdominal wall. The walls of the splenic arteries are uniformly thickened and inelastic. Two of the branches of the splenic, just as they enter the hilus of the organ, present at one side a large aneurysmal sac filled with old blood clot. At the hilus just beneath the capsule are felt three such sacs about the size of a small marble. On section these are found to be filled with old blood clot, the periphery of which is undergoing transformation into connective tissue. The spleen on section presents a rather dry appearance, with complete absence of lymphoid elements. In the center of the outer aspect is a small infarct about 1 x ½ cm., yellowish brown in color and completely cut off from the rest of the organ by a zone of dense connective tissue.

Pancreas. Of normal size and presents no gross lesions.

Kidneys. The right kidney is slightly larger than normally and weighs 240 gm. There is a marked chronic perinephritis, so that the fatty and true capsules are densely adherent. On the outer aspect of the organ is a mass the size of an egg. On section what is left of the kidney appears to be compressed by this large hematoma, consisting of clotted blood which occupies a fibrous sac on the outer aspect of the organ. On its periphery the hematoma is limited by the fibrous capsule of the kidney. It is apparently a false aneurysmal sac belonging to some vessel in the cortex of the organ. It is roughly the size of an egg. The rest of the deformed organ presents on section a yellowish-pink appearance and is dense in consistency. The cut surface is glassy; the cortical markings are completely obscured. The arteries, including the interlobular and arcuate, show a thickening of their walls and in a few places an aneurysmal dilatation. The latter, as well as nearly all the branches of the renal arteries in both cortex and medulla, are occluded by a recent thrombus. The left kidney is about one-half the normal size and weighs 125 gm. The capsule strips easily, disclosing a reddish surface which is everywhere studded with smaller and larger yellowish-white scars. The ureter

and pelvis are implanted in the center of the anterior aspect. The organ is of a dense elastic consistency and on section presents an irregular narrowing of the cortex, due to the above described scars, apparently the result of old infarctions. The cortical striations are rather obscured. Here and there throughout the cortex the arcuate, interlobular and larger branches of renal artery are thickened and along their course present occasional spherical aneurysmal sacs. On cross-section of the kidney these are seen to vary in size from a pinhead to a few which are about the size of a pea. All are filled with red thrombus, apparently deposited some time ante mortem.

Adrenals. Of normal size. Cortex narrow and contains relatively little lipoid material. The organ otherwise shows no abnormalities.

Gastro-intestinal Tract. Stomach: The entire mucosa is intensely congested and on the posterior aspect near the lesser curvature shows four shallow ulcers. The largest is the size of a thumb nail. The base of these ulcers is apparently formed by the muscularis and in the base are seen both recent and old hemorrhages. The edges of the ulcers are neither thickened nor undermined. Along the lesser curvature both the coronary arteries and the gastric branch of the gastroduodenalis artery are thickened and present along their course eight or nine aneurysmal sacs. About five of them, which are the largest, are along the course of the coronary artery. The very largest is about the size of a small grape. They are filled with red thrombus, which is undergoing organization. The entire mesentery, especially of the small intestines, is studded with numerous nodes varying in size from a pinhead up to a few the size of a small grape. They are lying along the branches of the mesenteric arteries, most of them being about one to one and a half inches from the intestinal insertion of the mesentery. Others are found in various places in the mesentery, a few also on the surface of the intestine at the mesenteric attachment. The intestinal tract, however, aside from irregular patchy congestion of the mucosa, shows no circulatory disturbances.

Brain. Shows no gross changes.

Systemic Arteries. Including the aorta they show moderate thickening of the wall and loss of elasticity. In the aorta are a few small patches of atherosclerosis beneath its intima. As to the frequency of occurrences of periarterial nodes along the course of the systemic vessels, nothing can be said because of the limited permission for the autopsy. Only a few small pieces of brachial and temporal and intracranial vessels could be excised for microscopic study.

Microscopic Examination. Numerous sections were made from each organ and from arteries and veins in various parts of the systemic, splanchnic, coronary, intracranial and pulmonary circulation. The material was studied with hematoxylin-eosin, Van Giesen and Weigert's elastica stains.

I. *Branch of the Superior Mesenteric Artery Which Was Removed at the Operation* (June 19, 1919). The section shows a fusiform dilatation of the artery, the lumen of which still contains fluid blood. In the wall of this vessel the lesions consist of two types: (1) An acute and subacute inflammatory process in the adventitia on one side of the vessel. Both the adventitia and the periarterial connective tissue at this side are extensively and densely infiltrated with small round cells, plasma cells and polynuclear leukocytes. The relationship of this inflammatory lesion to the vasa vasorum cannot be definitely ascertained. (2) The second conspicuous lesion consists in a remarkable homogeneous appearance of the media throughout the greater part of the circumference of the vessel, which gives the appearance of an actual necrosis of the muscle fibers in this coat. Here and there in this degenerated media there are collections of round and polynuclear leukocytes. Scattered through the degenerated media are fibroblasts which are apparently undergoing some proliferation. The damage has apparently occurred so acutely that the intima as yet shows no changes.

II. *Aneurysmal Node from Intercostal Artery* (Removed July 17, 1919). The vessel shows an extensive sacculated aneurysmal dilatation, the lumen of which is occluded by a mixture of blood-platelet thrombus and red clot. The wall of this aneurysmal sac for two-thirds of its circumference consists of dense connective tissue, whereas in the other one-third of the circumference the various layers of the arterial wall can still be made out. Here, however, the musculature of the media is markedly atrophic, and between these scattered muscle fibers is a peculiar bluish staining material, apparently a hyaline form of degeneration of connective tissue. In the expanded two-thirds of the circumference the wall consists solely of dense connective tissue which contains a large hemorrhage, probably a dissecting aneurysm. The elastic-tissue stains show no elastic tissue fibers in this part of the wall. Only in the small segment previously described as presenting some remnants of the structure of the arterial wall are still to be seen some strands of elastic tissue undergoing marked fibrillar degeneration.

III. *Autopsy Material* (October 8, 1919). Heart Muscle, Left Ventricle: Muscle fibers are rather thin and atrophic. The striations are poorly marked and there is considerable bipolar pigmentation. The small arteries in places show a slight uniform thickening of their walls.

Heart Muscle, Left Ventricle: This section has been taken perpendicular to the serous surface and in addition to the thickness of the ventricular wall contains the visceral layer of the pericardium and several large arteries. These vessels present a remarkable appearance. In places the arterial wall is enormously thickened, due to a productive inflammation in the media and intima. The thickened area consists of young interlacing fibroblasts lying in a

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peculiar pale blue staining intercellular substance. The media at this site shows a replacement of large areas of muscle fibers by the same peculiar pale bluish substance containing occasional young fibroblasts. At times this degenerative process involves the inner part of the media, in other places the peripheral part, whereas in still other sites it forms a patchy streaking throughout the musculature of the media. The process appears to be the end-stage of some degenerative phenomenon in the media, which has resulted subsequently in a compensatory proliferative and nodular thickening in the intima. The adventitia shows relatively little change. Where the thickening of the intima and scarring of the media are most marked the adventitia is often involved by a dense connective tissue in which small collections of round cells are to be found. The vasa vasorum occasionally show a uniform thickening of their walls and occasionally show a small tendency toward round-cell infiltration in their immediate vicinity.

Deeper in the heart muscle, branches of the coronary arteries just described show in places a similar involvement. In one such branch almost the entire vessel has been replaced by a loose connective tissue, leaving only a minute lumen in the center. In this small vessel the structure of the media has been almost completely obliterated by dense hyaline connective tissue. In addition to the changes described in the last section the heart muscle presents occasional small areas of interstitial scarring.

Coronary Artery: This section passes through the site of one of the small aneurysms on the descending branch of the left coronary artery. The greater part of the circumference of this structure is occupied by old, dense, connective tissue, muscle fibers of the media being present only in one small segment of the circumference. The entire lumen of the vessel has been closed by a recent blood clot which on its periphery is undergoing active fibroblastic invasion. The vessel looks as if it had undergone a marked uniform expansion previous to the occurrence of the thrombosis. Weigert's elastic stain shows an almost complete disappearance of all the elastic tissue in the vessel wall, no trace of the internal elastic membrane being visible. Only in the periphery, in the adventitia, are small elastic fibers to be discerned.

A second section, also through the thrombus of the coronary artery, presents almost an identical picture except that in one-half of the circumference of the vessel the muscle fibers of the media are still fairly well preserved. The rest of the media in this portion of the vessel wall, especially the peripheral layer, has been replaced by an enormous mass of loose connective tissue consisting of thin spindle-shaped fibroblasts running circumferentially in a peculiar granular blue-staining intercellular substance. This bluish staining material is probably the remains of a degenerative process. One of the small vasa vasorum in the region has been completely closed by young vascular connective tissue and then recanalized.

Small Descending Branch of Right Coronary Artery Near the Apex of the Heart: This vessel, which grossly appeared to be a sacculated aneurysm, appears microscopically to consist chiefly of a completely organized thrombus which has been recanalized. The wall of the vessel consists chiefly of old, dense, connective tissue, only a narrow band of muscle fibers being still present three-quarters of the way around the periphery. The internal elastic membrane is ruptured and shrunken so that it can be traced less than half the distance about the circumference of the vessels. The portion that remains is thin and atrophic and in places has undergone a fibrillar degeneration. In the other half of the circumference of the vessels only occasional small degenerated fragments of elastic tissue are to be seen.

Medium-sized Branches of the Coronary Artery: Show an irregular patchy scarring of the media, in places almost completely replacing the muscle fibers except for the circumferential ones on the periphery. The media shows an enormous nodular thickening, irregular in distribution. The internal elastic membrane shows a remarkable fibrillar degeneration which in places amounts almost to complete absorption. There is a small amount of newformed elastic fibrils in some of the scars in the media. In one place on the periphery of the vessel a rupture of the external elastic system has occurred.

Lung: Moderately anthracotic. Many of the alveoli as well as the interstitial tissue of the interalveolar septa contain heart failure cells. Pleura is moderately thickened by old, dense, connective tissue containing considerable anthracotic pigment. Here and there throughout the lung there is a considerable increase in the interalveolar connective tissue, but this is very irregular in distribution. The branches of the pulmonary artery appear to be normal. Some branches of the bronchial artery, however, show a fibrous thickening of the intima and media. The essential lesion in this lung, however, is a brown induration. In the elastic stains the bronchial vessels show an irregular fibrillar degeneration of the internal elastic membrane.

Liver: Marked parenchymatous degeneration, probably postmortem. There has apparently been an intense passive congestion. The centers of the lobules show marked dilatation of the sinuses, with atrophy and a brown pigmentation of the liver cells. In the periphery of the lobules the cells are large and are apparently undergoing some compensatory hypertrophy. The small branches of the hepatic artery in this section show no change. Liver capsule is slightly thickened.

Hepatic Artery, Medium-sized Branch: Shows an advanced degree of the characteristic pathological changes described in the coronary artery. The media is diffusely studded with bluish staining scar tissue. There is a similar irregular fibrous thickening of the

intima. In another medium-sized branch the patchy scarring of the media is found to be chiefly in the circular coat. In this branch the lumen is completely closed by dense connective tissue, apparently an organized thrombus. Between this dense connective tissue and the circular coat of the media there is a zone of pale blue staining material, homogeneous in character and containing a few fibroblastic nuclei. This is probably merely a degenerated connective tissue. The elastic stain shows that there has been a marked fibrillar degeneration of the interstitial elastic membrane which has ruptured so that it can only be traced about two-thirds of the way about the circumference of the artery. On the side where rupture of the elastica has taken place the vessel wall has undergone a bulging so as to form a shallow, sacculated aneurysm.

Spleen: Marked dilatation of the sinusoids and lymphoid hypoplasia. The trabeculæ show a marked thickening. On one large septum there has been a tremendous increase in dense connective tissue and in the center are the remains of old extensive hemorrhage. In places the reticular tissue is distinctly increased. Many of the smaller vessels show an irregular hyaline thickening of the intima, but no typical changes.

Splenic Artery: This is one of the main branches of the splenic. It is completely occluded by a mixture of blood-platelet thrombus and red clot. The thrombus is beginning to undergo organization at the periphery. Almost the entire media is replaced by old connective tissue, some of which stains bluish in the hematoyxlin-eosin preparation. As a result of this diffuse fibrosis of the media no line of demarkation can be made out between the intima and the media. In the Van Giesen stain some muscle fibers are still found to be present in one-half of the circumference of the vessel, but these can only be positively discovered in the peripheral portion of the circular layer and in the longitudinal layer. On one side of the vessel a tremendous expansion has apparently so thinned the wall that it merely consists of a narrow layer of dense fibrous tissue which is apparently upon the point of rupture. Although the entire vessel wall has been stretched by this aneurysmal dilatation the bulging of the wall is more marked at this particular point. The elastic stains show practically a complete disappearance of all elastic tissue in this vessel wall.

Pancreas: Shows a moderate degree of chronic diffuse interstitial pancreatitis. In the interstitium is one vessel which is completely occluded by old, dense, connective tissue taking a pale blue stain and containing relatively few fibroblastic nuclei. This organized thrombus has been partly recanalized. On the periphery it fades off into pink staining scar tissue of the media. Only in the periphery of one-half of the circumference of the media are there any muscle fibers. In the other half of the circumference the fibrous wall had apparently undergone a marked aneurysmal dilatation

before the lumen became thrombosed and the thrombus organized. The elastica can only be traced in the former half of the vessel and shows a fibrillar degeneration. The other half of the circumference contains no elastic tissue, apparently due to a rupture of the internal and external elastic membrane before the aneurysmal bulging took place. Other smaller vessels show similar though less marked changes.

Stomach: The sections show a shallow ulceration the base of which consists of acutely inflamed submucosa. The polynuclear leukocytes infiltrate downward into the musculature. Some of the small arteries in the submucosa in this region show fibrous scarring of their media. Near one such vessel there is an old hemorrhage.

Branch of the Superior Mesenteric Artery: The vessel shows a uniform expansion to about three times its normal diameter and is occluded by a mixture of blood-platelet thrombus and red clot, the former of which is already undergoing fibroblastic invasion. The media of the vessel, except in its most peripheral portion, is completely replaced by a dense, hyaline, connective tissue. Throughout the entire circumference no trace of an elastic membrane is to be seen in the Weigert elastica stains; in fact, all elastic tissue has disappeared from the vessel wall except for the irregular fibers which normally are present in the adventitia.

Branch of the Inferior Mesenteric Artery: Shows changes similar to the previous one, namely, aneurysmal dilatation which has recently been followed by thrombosis and beginning organization of the clot. The musculature of the media has been almost completely replaced by hyaline connective tissue in which the elastic system has completely disappeared. Some smaller branches in the section show a patchy scarring of the media at some one place and thickening of the intima opposite this site. The elastica in these smaller vessels is well preserved except on the diseased side of the vessel, where fibrillar degeneration has taken place.

Kidney: Presents a remarkable appearance throughout most of the cortex. The tubules have shrunken to solid cords, consisting chiefly of nuclei which are buried in a dense connective tissue. The glomeruli are everywhere well preserved except for a moderate dilatation of Bowman's capsule. The cause of the remarkable atrophy of the tubules with subsequent replacement fibrosis is to be seen in the extensive disease of the arteries throughout the sections. This is very similar to that which has previously been described, consisting either of patchy scarring of the media or a more or less complete replacement of the muscle fibers of the media by hyaline scar tissue which often takes a pale blue stain in the hematoxylin-eosin preparation. The medium-sized and larger branches are most extensively involved, though even the interlobular and arcuate arteries show extensive disease amounting often to complete occlusion due to narrowing of the lumen or to throm-

bosis. Many of the medium-sized vessels, down to arteries the size of the interlobular, often show aneurysmal dilatation either fusiform in shape or sacculated due to bulging of one side of the vessel wall. Many of these aneurysms are thrombosed and the thrombus more or less completely organized. The elastica stains show varying degrees of fibrillar degeneration in all the arteries. In vessels which are most extensively diseased this amounts to complete disappearance. In vessels in which no dilatation and no thrombosis have taken place the lumen is often markedly narrowed due to the tremendous increase in hyaline connective tissue in the intima. It is this gradual reduction in the blood supply which has apparently been responsible for the atrophy of the tubules, the more or less diffuse fibrosis and the subsequent shrinking of the organ.

Renal Artery: This shows very much less disease than do the smaller branches just described in sections of the kidney. There is some patchy scarring of the media. In the Weigert elastic stain the internal elastic membrane shows a fairly marked fibrillar degeneration which is most pronounced at one side of the vessel where the intima shows a marked fibrous thickening.

Adrenal: Both cortex and medulla are of normal size, the cortex containing a normal amount of lipoid material. No vessel changes are discoverable.

Brachial Artery: Shows small patches of scarring scattered through the media. This, however, is not very marked. The elastic system is also well preserved. In one of the branches of the brachial, however, there is a large scar in the media at one side of the wall and an extensive fibrillar degeneration of the media which has here ruptured, permitting aneurysmal sacculation.

Brachial Vein: Shows no changes.

Common Iliac Artery: Shows peculiar pale blue staining material between the muscle fibers in the inner portions of the media. In the elastic stain this appears to be due to a fibrillar degeneration of the elastic tissue. In one-half the circumference of the vessel this degeneration of the media is most marked and there is extensive hyaline thickening of the intima. In places this thickening of the intima appears to be of an atherosclerotic nature in that it contains masses of cholesterin.

Aneurysmal Node on the Temporal Artery: This appears to be an aneurysmal expansion of the vessel whose walls are extensively degenerated. Very few muscle fibers can be found in what remains of the media, which consists almost entirely of hyaline connective tissue, in places taking a pale blue stain. The lumen of this aneurysmal sac has been occluded by a thrombus of the blood-platelet type, which is about two-thirds organized. In the vessel wall one cannot differentiate between the intima and media, especially as the elastic stains fail to show even a trace of the internal elastic membrane.

Vertebral Artery: Shows only occasional small patches of scar-

ring in the media. The intima is markedly thickened and the internal elastic membrane shows a very extensive fibrillar degeneration, especially on one-half of the circumference.

Middle Meningeal Artery: Here the same degenerative processes are to be seen in the media and on one side of the vessel wall. There is a very marked fibrillar degeneration of the internal elastic membrane which has ruptured. An extensive thickening of the intima at this side has, however, apparently prevented rupture of the vessel wall or sacculated dilatation.

Summary of Pathologic Studies. In the branch of the superior mesenteric artery removed at operation on June 19, 1919, while the patient was still in the acute stage of his illness, the lesion was essentially an acute and subacute inflammatory process involving chiefly the adventitia and the periarterial connective tissue. This periarterial inflammatory process was associated with and probably directly responsible for a true necrosis of the muscle fibers in the media of the vessel. Although we were unable to prove the mechanism of this necrosis, we believe it to have been due to occlusion of the circulation in the vasa vasorum by the periarterial inflammatory infiltration.

In the material removed one month later, on July 17 (an aneurysmal node of an intercostal artery), little evidence of an acute inflammatory process could be discovered. The lesions were similar to those found in the arteries at autopsy.

At the autopsy which was performed three and a half months after the operation (October 8) the disease was found to involve all the systemic vessels, including the coronary, splanchnic, bronchial and cranial arteries. Vessels the size of the brachial and common iliac arteries showed the least damage, the most extensive lesions being found in medium-sized arteries, such as main branches of the renal, splenic, coronary, intercostal and superficial temporal. Much to our surprise no trace of the acute periarterial inflammatory process, which was so conspicuous in the material removed at the operation, could be found in spite of an extensive search. The vascular lesions as they existed after death apparently represented the end-stage of the disease, namely (1) extensive fibrillar degeneration of the internal elastic membrane amounting in some vessels to complete absorption, (2) fibrous-tissue replacement of the degenerated muscle fibers of the media, and (3) compensatory thickening of the intima, apparently a vain attempt to strengthen a much weakened arterial wall.

The intense degeneration of the elastica and the fibrous scarring of the media often resulted in rupture of the former and stretching of the latter, so as to form a sacculated aneurysm on one side of the vessel. When this did not occur the compensatory thickening of the intima on the side of the vessel, which presented the more extensive degeneration of elastica and fibrosis of the media, often gradually narrowed the lumen until the vessel was completely occluded or

finally became obstructed by the formation of a blood-platelet thrombus.

This case is remarkable because the vascular lesions found at autopsy represent the end-stage of a periarteritis nodosa, in which the acute periarterial inflammatory process has long subsided and the disease was progressing toward healing. Death occurred from renal insufficiency, due to the gradual atrophy of tubules and replacement fibrosis in the interstitium consequent upon the gradual and progressive reduction in the circulation through the diseased renal vessels. The one other case of similar nature in which all the arterial lesions found at autopsy had advanced to the stage of healing was reported by Spiro.[5]

From the standpoint of *etiology* our case is also important. It gives very positive support to the contentions of those writers who maintain that syphilis is not the cause of the disease. The two Wassermann tests which were made, one early, the other late, in the course of the illness were both negative, and, furthermore, nothing of a syphilitic character was found in any of the pathological examinations. Syphilis, if it plays any role at all, is purely secondary. Klotz, Dickson and Spiro have discussed this point very fully and we agree with their conclusion that syphilis may have had some predisposing effect on the bloodvessels in the patients in whom it was present. It is true that a number of cases have been reported (Benedikt, Schmorl, Lamb, Klotz, Spiro and others) in which the Wassermann test was positive, yet nothing of a luetic nature was found in the gross or histological specimen. The pathological differences between periarteritis nodosa and syphilitic arteries are very great and spirochetes have never been demonstrated by any observer in the former. The fact that great improvement was noted after specific treatment in the patients of Benedikt and Schmorl has no significance, since Benedikt's case was never proved by autopsy, and Schmorl's case, on which so much stress has been laid, was very poorly observed and the report of it is very unsatisfactory. The only reference to it which we could find is that which is contained in a discussion on Benda's paper on specific arteritis before the Deutsche pathologische Gesellschaft in 1903, when Schmorl took exception to Benda's statement that periarteritis nodosa was not specific. His remarks, in full, are as follows:[7] "A fifty-three-year-old woman, who had had vague symptoms, developed nodules in the right lower abdominal region and right thigh. These were excised and proved to have all the characteristic of periarteritis nodosa. An energetic antiluetic treatment caused the rapid improvement of all the symptoms and the disappearance of the nodules on the right thigh. Two years later she died of an acute portal thrombosis. At the autopsy no changes could be found in the

[7] Verhandlungen der deutsch. pathologisch. Gesellschaft, 1903, 203.

vascular system which would correspond to those of periarteritis nodosa; what was found were residues of the same in the form of small fibrous foci in the kidneys, liver and heart, which were very closely related to the bloodvessels. He believed that the excellent results of the specific treatment would surely leave no doubt as to the syphilitic origin of the disease."

The fact that the patient improved under specific treatment is no proof at all, since the improvement may have been independent of this treatment, for in our own patient the pathological examinations of the autopsy material gave definite proof of healing without any such treatment. It is also to be noted that Schmorl's case was observed in 1903 before the days of the spirochete and salvarsan. Additional proof, if any is demanded, is afforded by the observations of Lamb, Spiro and others that a similar disease exists in stags and other animals.

It is true that one may easily fall into the error of confounding specific arteritis with periarteritis nodosa. We are indebted to Dickson, who laid the greatest stress on the necessity of the differentiation of the two conditions. He even went so far as to propose a new name, polyarteritis nodosa acuta, for the cases of true periarteritis nodosa and to allow the latter name to be used for the cases which are syphilitic. This suggestion has wisely not been adopted, as it would only cause added confusion, and the name originally proposed by Kussmaul is too firmly established to be discarded.

It is to be regretted that our case has shed no light on the possible bacteriological relations of the disease, for aërobic and anaërobic blood cultures which were taken during life were sterile as well as all the cultures from the various nodules. All the other blood cultures which have been reported have also been sterile. But the same cannot be said concerning the nodules from the cultures of which a variety of organisms have been obtained. These include streptococci, staphylococci, Bacillus coli and Bacillus influenzæ. These varied results tell their own story and it is needless to add to the discussions of this topic which have already been published by Lamb, Klotz and Spiro. Their findings and their animal experiments have led to no definite results. As regards Klotz's suggestion of the possible relations of the Streptococcus viridans, it is to be noted that it was absent in the throat cultures in our patient and it was never found in any of the other bacteriological examinations.

Nevertheless, all the evidence which has been presented would indicate that the disease is of an infectious nature, the cause of which is as yet unrecognized, and which, for some unknown reasons, attacks the walls of the medium-sized arteries, with a predilection for the mesenteric, renal, hepatic, pulmonary, cardiac and cerebral vessels, as well as those in the skin and in the muscles of the extremities. After a time, if the patient survive, these structural changes become less marked and undergo involution; the symptomatic

evidences of the acute infection become less marked and finally disappear. Death in the cases of long duration is caused by the structural changes which have been left behind in the tissues attacked. Thus our patient made a symptomatic recovery from his periarteritis nodosa, but died of the resultant nephritis.

Closely allied to the question of the etiology are those of whether the periarteritis nodosa is a disease entity and whether there are similar changes in the arteries in other conditions. These subjects have been carefully considered by Klotz and Spiro. In his discussion Klotz emphasizes the importance of the perivascular lymphatics in the study of the distribution of bacteria in and about the walls of the vessels: "It is not uncommon to observe the advance of infection and inflammation in tissues surrounding the small arteries of the mesentery of the appendix. It is probable that the thromboses so commonly occurring in the vessels of these outlying tissues have their cause in the damage induced through infections of the arterial coat arising from the perivascular involvement. The same perivascular responses are also observed in the Fallopian tubes, the broad ligament, the umbilical cord and elsewhere. . . . This migration of the inflammatory exudate is not a condition which, *per se*, tends to follow the artery, but which, because of the lymphatics, is the line of least resistance in this process. This is true not only of infections of the suppurative type but also of the non-suppurative lesions. Of the latter it has been frequently demonstrated that the infections associated with acute rheumatic fever and the various rheumatoid processes are for the most part periarterial in their distribution. The focal inflammatory deposits that are so constantly found in the myocardium in rheumatism are excellent examples illustrating the localization in the lymphatic spaces and channels of the nutrient vessels. Thus we are led to believe, and we have further demonstrated in experiment, that periarteritis nodosa differs from the common periarterial inflammations only in the peculiar manner of the damage in the arterial wall. The distribution and the progress of the disease along particular branches of arteries are not unique for this lesion which has received a special name."

Spiro also takes the view that periarteritis nodosa is not a disease, *sui generis*, and he directs attention to the similarity of the nodules to those which occur in the coronary artery as described by Wiessel[8] and Wiesener.[9] Spiro believes that periarteritis is not a distinct entity but that it belongs to the category of mesarteritis which may result from various infective agencies. The cases which run an acute course are those which occur in individuals who have weak vascular systems either congenitally or as the result of overexertion, increased blood-pressure or possibly neuropathic changes.

From the clinical side our patient was also most interesting. The

[8] Wiener klin. Wchnschr., 1906, 726.

[9] Ibid., 723.

striking feature was the occurrence of abdominal symptoms which simulated those of an acute surgical condition. This simulation of an acute surgical condition can readily be understood when we recall that the branches of the celiac axis are the most frequent site of the lesions. These abdominal pains may occur at any time during the course of the disease and may even usher it in. The frequency of this mode of onset is estimated at 25 per cent. by Lamb in the series of cases which he studied. Abdominal symptoms may also be the leading complaint during the course of the disease, and abdominal pain of some kind is present at some time or another in nearly all the cases. The pains come on in severe colicky attacks and are usually referred to the upper abdomen. They may also be felt in the region of the kidney, or they may be diffuse pains all over the abdomen. They may be localized or they may radiate to the back. These attacks may last several days and are usually associated with abdominal tenderness and distention. If to this local picture we add the general symptoms of fever, a very high polynuclear leukocytosis and albuminuria we need not wonder that these patients are suspected to be suffering from an acute surgical condition. That the severe attacks of abdominal pain were the leading feature of our patient's complaints was evidenced by his admission to the surgical division when he applied for relief. Although he was under very careful observation for two weeks no definite conclusion could be reached with such a varied array of symptoms, and he was finally operated on with the expectation of finding some unusual condition in the upper abdomen.

This type of the disease is also well shown in Lamb's Case II: A girl, aged ten years, had a sore-throat and acute abdominal symptoms nine days before admission to the hospital. When admitted she had a fever of 102.6° and a leukocytosis of 33,000 with 93 per cent. polynuclears. A diagnosis of acute appendicitis was made and she was operated on. The appendix and peritoneal cavity were found to be normal and nothing could be found to explain the acute abdominal symptoms. Both of the cases reported by Klotz have interesting abdominal features, and it is a curious coincidence that in both patients death resulted from hemorrhages into the peritoneal cavity from ruptured aneurysmal sacs. His first patient was a woman, aged thirty-three years, whose final illness was four weeks in duration, beginning with a severe cold which followed exposure. Her chief complaints were pains in the muscles and joints; later on she had intense, cramp-like pains in the abdomen. She ran a low, continuous temperature and had albuminuria, a slight icterus and a leukocytosis of 12,000, with 76 per cent. polynuclears. In the presence of a tender and palpable gall-bladder a diagnosis of empyema of the gall-bladder was made. The contemplated operation was deferred, as the patient improved very much. On the following day (six days after the onset of the acute abdominal

symptoms) she suddenly went into collapse and died. The autopsy revealed the typical lesions of periarteritis nodosa, with aneurysms on the hepatic and cystic arteries. One of the aneurysms on the hepatic artery had ruptured and had led to an extensive hemorrhage about the liver and into the peritoneal cavity.

Klotz's second case was equally unusual, and by a curious coincidence occurred within a month of the first one. A fifty-three-year-old man was admitted for vague symptoms and a history of not feeling well for a year and a half. A recent cold had accentuated these symptoms. Two weeks after admission he had a slight fever, a sore-throat and a purpuric rash on the legs, thighs and chest wall which suggested erythema nodosum. One of these nodules became larger and fluctuating. On incision a thick, brownish gelatinous material escaped. The cultures from it were sterile. From the time of the onset of the tonsillitis he ran a low, continuous fever; there was a leukocytosis of 13,000. The blood Wassermann was four plus. Some of the nodules which suggested erythema nodosum disappeared and new ones came. One of these nodules was excised, but a diagnosis of the arterial lesion could not be made, owing to the extensive disintegration and hemorrhage which were present in the excised tissue. Cultures from the excised nodule and the blood were negative. Clinical manifestations of an intra-abdominal condition were not present, his main complaints being those of a decompensated heart. After a five-weeks' stay in the hospital he died rather unexpectedly, although during the last week he became progressively weaker. At the autopsy a very extensive periarteritis of the branches of the celiac axis was found, together with a hemoperitoneum; the latter was the result of hemorrhages from the vessels of the gastrocolic omentum and pancreas. The nodules in the skin were also due to periarteritic nodosa changes. Chronic endocarditis, evidently of long standing, and syphilitic cirrhosis of the liver were also found.

The subcutaneous nodules are most important in making the diagnosis. In the few cases in which the diagnosis was made during life it was only established by means of them. Ours is the only case in which it was reached without them. Unfortunately they are present in only 25 per cent. of the cases. It is interesting to note that the diagnosis may be missed even when they are present and examined for diagnosis in a suspected case, as happened in Klotz's Case II. The subcutaneous nodules are small and firm and feel like shot along the course of the artery; they are quite superficial. They have been found in the face, neck, thorax, abdomen and extremities. They are usually painless; rarely are they inflamed and tender. Pulsation is seldom observed in them, as thrombosis occurs early. Very rarely their size is larger than a pea; a few have been reported which reached the size of a hazelnut. In Benedikt's case, besides other nodules, there was a tumor the size of a fist in the lower right abdomen. As this simulated an appendicular abscess an

operation was performed. The mass proved to be an intramuscular hematoma due to the rupture of an aneurysmal sac on one of the intramuscular arteries. They rarely suppurate; the only exceptions are the two instances which have just been referred to.

A maculopapular rash was also present in our case. Eruptions of the most varied types have been reported by other observers; they are either hemorrhagic or toxic. They may usher in the disease or they may occur later on in successive crops. Desquamation of the entire body without a preceding rash has also been reported. These rashes, when associated with the other confusing general symptoms, are most misleading and the possibility of their occurrence should be remembered in a suspected case. The other skin manifestation which deserves notice is edema, which may involve the ankles, the face or the entire body. In some form or another it has been observed in a large majority of the cases. As nephritis is so frequent in this disease it is a fair inference to assume that it is renal in origin.

The very high leukocytosis deserves special mention. In our patient it ranged between 30,000 and 50,000 in the acute period, and long after the fever had subsided it persisted at 20,000. Even in the terminal stages when, as the autopsy showed, the vascular lesions were far advanced in the process of healing it was still as high as 13,000. Blood counts have only been reported in the cases which have been observed in the last decade; they have uniformly been very high. The polynuclear cells have also been very high in the percentual relation. We wish to direct attention to the possible diagnostic value of these high white cell counts in doubtful cases of irregular pains, especially in the abdomen, when associated with fever and doubtful rashes.

Pains in the voluntary muscles and along the peripheral nerves are also important symptoms which are rarely absent. They may be so pronounced as to lead to the suspicion that the case may be one of poliomyositis or trichinosis. Indeed, in the classical case which gave the disease its name, Kussmaul believed that he was dealing with an unusual type of trichinosis until the development of atrophies and other symptoms convinced him of his error. The pains in the muscles are of varying degrees of intensity and may be tearing or cramp-like in character. There may also be pains in the joints. Lamb noted their occurrence in 39 per cent. of his series. They may be acute enough to simulate acute articular rheumatism, especially if several joints are involved.

Attacks of tonsillitis or a history of sore-throat are reported in so many cases that attention should be directed to the throat in any discussion of this disease. Recurrent attacks of tonsillitis or quinsy are of frequent occurrence in the previous history, and the patients often refer the beginning of their illness to an attack of sore-throat. This is well demonstrated in our own case and in those reported by Lamb and Klotz.

Lamb has directed attention to the fact that symptoms and physical signs referable to the heart are strikingly absent, although the coronary arteries are so frequently involved. We can corroborate this statement, and it is difficult to conceive that a heart whose structure was so extensively diseased as shown by the pathological studies should have functionated so normally.

It is also surprising that the case records which have been published do not show more evidences of renal involvement, since the small arteries of the kidneys are attacked in nearly every case. In Lamb's series of 38 cases no mention of the urine is made in 10 cases. In 5 it is definitely stated that albumin was not present. Often, however, there was only one examination, and the condition of the kidneys at the necropsy indicated that albumin would have been found if repeated examinations had been made. In 23 cases, or 82 per cent. of those in which the condition of the urine is given, albumin was present, generally in moderate amount, but varying from a trace to as high as 6 per cent. In the cases in which repeated examinations were made albumin was not always present but showed exacerbations and remissions. In 14 cases casts, generally hyaline and granular, were present. Blood was reported in 9 instances.

Our case sheds some light on these apparent discrepancies and demonstrates that the condition of the urine does not necessarily correspond with the changes in the kidneys. That the kidneys had been involved early in the course of his disease is evidenced by the severe attacks of renal pain and ureteral colics and hematuria, which made him seek relief at the hospital. The urine was negative, however, save for a few red blood cells. And this in the presence of a marked nitrogen retention in the blood, *i. e.*, urea nitrogen, 35 mil.; incoagulable nitrogen, 95 mil.; creatinin, 2 mil. The urinary evidences of the nephritis did not appear until he had been in the hospital for five weeks, and even then the urinary changes were only those of a mild nephritis. The eye changes, however, appeared very early. But when he returned to the hospital after an absence of only three weeks, so rapidly had the disease in the kidneys advanced that he presented the appearance of an advanced nephritic, from which he died within five weeks.

The alluring temptation to enter into a discussion of the diagnosis and differential diagnosis of periarteritis nodosa must be resisted. Our case has not made this task less difficult. The reader is therefore referred to the publications of Schroetter, Dickson, Longcope, Lamb and Klotz, where the subject is well presented. How difficult the diagnosis of this disease may be is well demonstrated by the experience of Klotz. Although he had encountered a case in which the diagnosis had been established by the postmortem examination only a month previously, yet the examination of an excised nodule failed to verify the correct suspicion in his second case.

URTICARIA, CLASSIFICATION OF TYPES AND ITS CAUSES.

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It has been shown by Walker,[1] Rackemann,[2] Talbot,[3] Fordyce,[4] Blackfan,[5] Fox and Fisher[6] and many others that protein hypersensibility in predisposed persons is a cause of asthma, hay fever, eczema and urticaria. The etiologic information that has been obtained by cutaneous reactions to various proteins exceeds all others and has made it possible to actually cure some of the cases and relieve a number of others.

The causative agents in urticaria seem to be closely related to those of the above diseases. It is a common experience to find one or more associated in the same individual or family. Often when studying asthma, hay fever or eczema, hives may suddenly appear and relief of the foregoing disease may cure the urticaria. From this close relationship one naturally thinks of studying urticaria along the lines of protein sensitization.

From the number of cases seen in my practice and that of others with whom I have been associated I have been able to select cases which show the manner in which protein sensitization may occur. I have tentatively drawn a graphic chart, after the plan of Walker for asthma, which I will show later. In cases studied I have not confined myself to cutaneous tests alone but have had the benefit of careful examinations, special investigation for evidence of focal conditions and roentgen-ray studies. A combination of such evidence is necessary to make intelligent skin tests.

Types of Urticaria.—The following classification of urticaria is based upon etiologic lines. I have found it of assistance as a means of study:

URTICARIA.

- Non-sensitive to proteins:
  1. Neuropathic.
  2. Chemical.
  3. Constitutional.
- Sensitive to proteins:
  - Seasonal:
    1. Pollens.
    2. Bacteria.
    3. Foods.
    4. Animal proteins.
  - Non-seasonal:
    1. Foods.
    2. Bacteria.
    3. Animal proteins.

[1] Causation Urticaria, Eczema and Angioneurotic Edema by Proteins Other than Those Derived from Food, Jour. Am. Med. Assn., March 30, 1918, lxx, 897.

[2] Specific Treatment of Hay Fever, Boston Med. and Surg. Jour., March 18, 1920.

[3] Eczema in Childhood, Med. Clinics of North America, January, 1918, p. 983.

[4] Cutaneous Reactions from Proteins in Eczema, Jour. Cutan. Dis., 1911, xxix, 129.

[5] Cutaneous Reaction from Proteins in Eczema, Am. Jour. Dis. Children, May, 1916, p. 441.

[6] Protein Sensitization in Eczema in Adults, Jour. Am. Med. Assn., October 2, 1920, 75, 14, p. 907.

It can thus be shown that urticaria may occur as a result of protein hypersensitization or otherwise. There seems to be a need of classifying the sensitive type further into seasonal and non-seasonal. For instance, in the seasonal type urticaria may be brought on by inhalation or contact with pollens. In certain seasons epidemic infections are numerous and hives may occur from this cause. Recent cases were reported associated with the epidemic of influenza. Stokes[7] reported cases that occurred following the administration of influenza vaccine. Certain food, fruits, vegetables and seafoods are seasonal and therefore included in both groups. Animal sensitiveness is placed in both divisions, as it may be seasonal from close relationship by being indoors, or in certain other seasons when on vacation in summer resorts, mountains, etc. In the non-sensitive column I have made some rather broad classifications.

Under No. 1 of the neuropathies I have placed the cases seen in which psychoneuroses, hysteria and neurasthenic conditions without discoverable organic or protein sensitization were present. The chemical group had to be represented on account of the fact that certain chemicals when applied locally will produce hives.[8] I have seen hives associated with organic conditions as nephritis, goiter, etc., and so far as I could prove, metabolic disturbances were the cause. I realize that in the non-sensitive group there is need for a broader understanding and the classification may be further extended.

Method and Specificity of Skin Tests. The cutaneous method has been used entirely by me. It is sufficiently sensitive and yet not too sensitive, without danger, simple, and is therefore the method of choice. It is briefly as follows:

"The skin surface, preferably the forearm, is cleansed with 40 per cent. alcoholic solution. Abrasions one-eighth inch in length are made with a sharp scalpel. A small amount of protein of food, animal, bacteria or plant in solution is placed thereon. Solution is either made by adding a drop of one-tenth sodium hydrate solution to the powder and mixing on abrasion with a toothpick or solution made on a watch-glass and placed on the cut. Within ten to thirty minutes, if the reaction is positive, a small wheal develops which may or may not be accompanied by an area of erythema and swelling. One of the abrasions is left as a control, and by this method a comparison of the natural reaction to a cut and the application of the soda solution may be obtained. Wheals less than 0.5 cm. in diameter are not considered positive. According to the amount of reaction a classification may be made from 1+ to 4+."

[7] Etiologic Analysis, Chronic Urticaria following Influenza Vaccination, Med. Clinics of North America, November, 1919, iii, 821.

[8] Sollman, J.: By Animal Aromatics and Urea Derivatives, Jour. Phar. and Exper. Therap., August, 1917, x, 147.

The above is briefly the method in common use, and under ordinary circumstances will be sufficiently clear in its reaction. Occasionally one meets with a dermatographic skin in which wheals will develop larger than 0.5 cm. in all cuts, or there may be some slight variation in the size.

In cases of multiple sensitization a wise plan is to make up various dilutions of the solutions, to which reaction occurred, and determine the amount of sensitiveness.

A positive reaction means that sensitization exists to foods parenterally. It does not prove that such a condition exists otherwise. This perhaps may explain why elimination of proteins has no effect on hives in some cases. In single sensitization it is more liable to be the cause. In children this is more prone to be true to certain classes of food. It has seemed to me that a wise plan would be to test a series of normal individuals to proteins to determine what proportion would give positive reaction without evidence of disease. By this method we have modified our ideas as to value of findings in other tests, particularly as to acidity of stomach contents. It would no doubt be found that a number would react from inherited tendencies. The method of exciting the latent sensitization would be next in order.

Urticaria from Foods.—In childhood it is a simple matter without skin tests to determine foods producing urticaria. The diet is simple and the outbreak often follows promptly from the addition of a new article. Eggs, wheat and oats are the chief ones to which children are most often sensitive. As has been shown by Blackfan in his studies of eczema a family history of specific sensitiveness to a certain food often exists. In adult life it can readily be seen that the determination is not so simple. I have found quite a number of adult cases to be sensitive to foods when applied to the skin, but have been disappointed in the results obtained when they were eliminated from the diet. In such a capricious skin condition it is very difficult to draw conclusions in regard to the effect of the withdrawal of certain susceptible foods. In the last eight cases I found multiple sensitization present. In all of these, in so far as could be determined, there was no change in the urticaria by eliminating the foods. I am quite sure others have met with disappointment in this respect, for I notice that McBride and Schorer[9] in their report of cases met with a number of failures. Also that Engmann in his work at the Children's Clinic, St. Louis, Mo., has had similar experiences. I am unable to explain the cause of the failures other than that there must be other factors and the food reactions are purely secondary. There have been a few cases examined in which favorable results have been obtained, as for instance in the following two cases:

[9] Urticaria and Erythema from Foods, Jour. Cutan. Dis., February, 1916, xxxiv, 70.

CASE I.—Child, aged two years. Was seen in May, 1920. Eggs were added to the child's diet for the first time that morning. One hour afterward the child broke out with giant hives. The child was sensitive to whole egg and egg-white by a skin test. Eggs were not added to the diet until August, when a small amount of egg-white was given and the child again broke out with less severe hives.

CASE II.—Female, adult, aged thirty-eight years, has had hives periodically for the past three years. They first came on while on a camping expedition in Canada. The diet contained at that time an excess of pork and beans. There was a family history of migraine. Skin tests were positive to beans, pork, beef and wheat. All were eliminated from the diet. The hives, which were present over various parts of the body at the time of the tests, cleared up within two weeks. The patient has had a slight return of the hives only when dietary restrictions have been broken.

Pollens as a Factor. Pollens as a cause of urticaria have not been considered to be a factor until within recent years. The following case exemplifies an urticaria brought on during ragweed pollinating season in all probability from mass ragweed protein inhalation:

CASE III.—Girl, aged fourteen years. Has had hay fever, commencing about August 15, for four years. Sensitive to ragweed in dilution of 1–10,000. For the past three years, within a week after onset, has had urticaria. Condition usually lasts about a week and subsides without treatment. The past two seasons has had some relief of hay fever by treatment. This year had hives only for one day.

Psychoneuroses. The nervous manifestations present in a number of cases cannot fail to attract attention. Osler stated in his report of cases that a family history of nervous disorders was present in angioneurotic edema. The following is an example of hives from a neurosis:

CASE IV.—Young married woman, aged thirty years, was seen February 5, 1920. Had had hives for five months before seeking relief. They appeared while on a boat trip. Lesions over various parts of the body. Highly neurotic disposition. Urine, blood Wassermann, blood sugar were negative. Roentgen-ray examination of the gastro-intestinal tract showed hypermotility and hyperperistalsis. Skin tests were positive to chicken, cheese, peaches, banana, pneumococci and Staphylococci aurei. No sources of infection could be discovered. The articles of food to which the patient was sensitive were eliminated from the diet, with no improvement. Dr. Finlayson made a neurologic diagnosis of psychoneurosis

and stated that he had been able to produce hives in this patient while in his office by any excitement to the nervous system, as by anger, fright, emotions, etc.

Focal Infection. Tonsils, teeth, sinuses and gastro-intestinal tract are most often the seat.

CASE V.—Miss H. was seen in May, 1920. Hives came on following rhinitis and sinusitis. Skin tests showed positive reaction to pneumococci and Staphylococci aurei. Operative measures to improve breathing space and sinus drainage were instituted, with relief of condition. The patient had had hives two weeks before being seen. Two months have passed and no return has occurred.

Injection of Foreign Protein. The most common example of this manner of producing urticaria is from the injections of vaccines or horse serum. Such a case as this is the following:

CASE VI.—Seen in January, 1920. An exudate had appeared on the patient's tonsils a few days previous and his physician injected antidiphtheritic serum. The throat cultures later proved to be negative. Following the injection a severe urticaria developed. Adrenalin relieved the condition entirely, but it soon reappeared and lasted for several days.

Conclusions.—A study of urticaria along the lines outlined by various writers for asthma, hay fever, eczema by means of cutaneous tests, using food, bacterial, animal and pollen proteins, will be a helpful procedure. It will be a means of discovering the sensitive type of cases. The classification of types of urticaria will be of assistance. Some common examples have been shown. While the results have been satisfactory in these cases a much larger proportion of non-sensitive cases has been encountered. In a large number of those sensitive to foods the elimination has failed to relieve the condition. No statistics are presented, but views are expressed covering a study of cases encountered during the past two years.

THE VALUE OF BASAL METABOLISM STUDIES IN THE DIAGNOSIS AND TREATMENT OF THYROID DISEASES.[1]

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BASAL metabolism studies, particularly in thyroid disease, have occupied the attention of many investigators and clinicians especially in the last few years, and out of these studies have arisen several

[1] Read before the San Francisco County Medical Society, September 14, 1920.

practical methods of determination of basal metabolism as well as certain definite conclusions as to the deductions which one is able to draw from such experimental work.

By the basal metabolism of an individual is meant that minimum chemical change resulting from the continuous organic cellular functions of the body which are essential for life. These chemical changes require oxygen, and it is possible by measuring the oxygen consumption by the body at complete physical and alimentary rest to determine the minimum heat production or basal metabolic rate for the individual. Thus the basal metabolism can be measured by calorimetric estimations of the heat production resulting from the continuous chemical changes in the body, either by direct computations of the heat given off, as is made possible by the large Atwater Rosa-Benedict apparatus, or by indirect calculations of it from the oxygen consumption by the body.

How gradually through the work of Lavoisier about 1780, Liebig about 1842, Voit about 1857, Pettenkofer about 1866, Rubner about 1885, and finally Atwater and Rosa about 1897, the basis of our present knowledge of metabolism developed, is outlined in Lusk's *Science of Nutrition*. Since then, through the work of Sonden and Tigerstedt, Jacquet, Grafe, Speck Zuntz, Geppert, Tissot, Douglas, Rolly, Benedict and Carpenter and DuBois, several types of apparatus for estimating metabolism by measuring the respiratory exchange have been constructed and many metabolic studies of adults and children in health and disease by many other investigators have been carried out.

Du Bois recently reviewed the history of basal metabolic studies in thyroid disease. Some of the noteworthy contributions to this phase of metabolism in which we are interested will be mentioned. Magnus Levy, in 1895, was first to demonstrate an increase in metabolism in hyperthyroidism and a decrease in myxedema. In 1899 Hirschlaff reported a severe case of hyperthyroidism, with autopsy findings, in which the rate rose to 105 per cent. above normal. In 1909 Bergman found a decrease in metabolism in myxedema and an increase after thyroid administration. The most important recent articles have been those of Du Bois, Means, McCaskey, Plummer, Boothby and Rowntree.

All investigators agree that basal metabolism depends largely upon thyroid activity and that an increase in the activity of this gland raises the metabolic rate above normal, while a decrease in thyroid secretion depresses the rate below its normal level. Other ductless glands, especially the pituitary and ovary control metabolism to a lesser degree, though certain diseases such as fevers, lymphatic leukemia, hyperpituitarism, polychemia, severe diabetes, cancer and pernicious anemia also increase the basal metabolism rate and starvation, hypopituitarism and wasting diseases decrease

it, all these conditions can easily be ruled out in a careful diagnostic study. Thus, for proper investigation, basal metabolic rate determinations in thyroid disturbances are coming to be recognized as being as indispensable as is the Wassermann reaction in syphilis or temperature determinations in fever.

Because of this recent recognition of the value of metabolic rate determinations in the study of thyroid diseases, two types of apparatus, namely, the Benedict portable respiration apparatus and the modified Tissot respiratory valve apparatus, have been perfected for the clinical estimation of basal metabolism. The Benedict type is so constructed that pure oxygen is kept circulating through the patient's lungs, the CO_2 being extracted from the expired air by soda lime and the metabolic rate being determined from the oxygen consumption which is read off directly from the spirometer scale. The Tissot type necessitates the collection of the expired air during a definite short period of time in a large spirometer, samples of which are later analyzed by the Haldane gas analysis machine for oxygen and CO_2, from which the oxygen consumption and the respiratory quotient are computed.

This Benedict type has gained considerable recent recognition as an instrument suitable for office estimations of basal metabolism through the articles of McCaskey and advertisements in the journal which recommend it for clinical use. Only casual mention has been made, however, of the modified Tissot unit which has been the instrument most commonly used by clinical men. The Tissot type has certain advantages not enjoyed by the Benedict. These are fewer connections, no necessity for electric current, no necessity of providing oxygen, no possibility of motor difficulty, no necessity of daily cleansing of spirometer and motor and no replenishing of soda lime and calcium chloride mixtures. Benedict and Carpenter both repeatedly state that the Tissot would be preferred to the Benedict in all cases were it not for the time-consuming and difficult gas analysis.

In regard to this analysis it necessitates, of course, care and accuracy, and because of this phase of technic with the Tissot, about three-quarters of an hour more time is consumed in the test than is necessary in the use of the Benedict. However, the Tissot type furnishes an accurate measure of the respiratory quotient and the CO_2 excretion, which is comparable, as Carpenter has shown, with that obtained with the universal respiration apparatus and which cannot accurately be determined with the Benedict portable type. Moreover, it must be realized that this metabolic work cannot economically be carried out by many men in any community and that the actual work will probably be done in most cases, by a well-trained technician, under the supervision of the clinician, to whom an extra hour of time will mean little, providing more accurate

and complete data are obtainable. The clinical applicability of the Tissot method is shown on a large scale at the Mayo Clinic, where several units are in operation all morning, and where the gas analyses are made by high-school girls under the supervision of Doctors Boothby and Sandeford.

The writer has been interested in basal metabolism in thyroid disease since 1915, when he came in intimate contact with the work of Means, Joslin, and Du Bois in Boston and New York. This interest was intensified last October when he watched the work of Boothby and Plummer at the Mayo Clinic. Since then the modified Tissot type of apparatus has been established in his office and it has been found to be most satisfactory for clinical use. He has followed the instructions given by Boothby in his recent monograph, both in regard to the manufacture of the spirometer, the setting up of the Haldane and the actual experimentation and computations.

Through the able assistance of Margaret Eakin we have made careful clinical and metabolic studies of some 80 cases of actual and suspected thyroid disturbances and have become convinced of the value of basal metabolic rate determinations as a guide to both the diagnosis and treatment of these conditions.

In the first place, *mild or definite cases of hyperthyroidism can be differentiated from neuroses and early tuberculosis, by basal metabolic rate determinations.* In a series of 49 cases referred to me, with the diagnosis of actual or suspected hyperthyroidism, only 16, or 39 per cent., had rates above the approximate normal limits of ±10 per cent. Clinically, all the cases showing rates higher than +10 per cent. were definitely hyperthyroid. Moreover all the other cases, with the exception of case 23, that showed normal metabolic rates had one or more symptoms and signs which suggested hyperthyroidism, though a very careful scrutiny of their records in most cases would incline one to doubt the existence of too much thyroid secretion. It is in these cases, especially where, as in Case 31, a decided exophthalmos was present, or in Case 1, where marked tachycardia, nervousness and sweating occurred, or in Case 22, where a tachycardia following a recent tuberculosis persisted, that a method of deciding on the responsibility or harmlessness of the thyroid gland is of great importance. We all see tremulous, nervous, excitable, weak and thin individuals who may or may not be hyperthyroid in type, the definite determination of which state is impossible without such a test as this one we are considering. Clinicians especially interested in heart diseases and in tuberculosis are beginning to see the advantage of these determinations in their diagnostic work. The basal rate determinations are being found of increased value in the analysis of tachycardias. Peabody was able by metabolic studies to confirm his impression that the thyroid was not causative in the etiology of the "Irritable Hearts of Soldiers." McCaskey, moreover, emphasizes the importance of this use of the

metabolic rate as a diagnostic procedure in these types of disturbances.

Again, the *severity of an obvious case of hyperthyroidism can be more accurately determined through basal metabolism rate determinations, than by any other method of analysis.* Thus in our series Case 14 had symptoms which could easily suggest a very severe state of hyperthyroidism, whereas her metabolic study placed her in the mild group of cases. Case 27 impressed one as suffering with extreme hyperthyroidism, and it was with much satisfaction I found him to be only in the severe type of the disease. Case 36 had encephalitis lethargica develop on top of her hyperthyroidism, and the problem of how much the thyroid was to blame for the prolonged convalescence and weakness was greatly illuminated by the basal metabolic rate result. Case 56, who had exaggerated symptoms and signs of hyperthyroidism, did not suggest before our metabolic rate study the unusually high rate of +128 per cent. Finally, Case 73, who one year ago had a marked struma with tachycardia, exaggerated tremor and loss of weight and had her septic mouth cleaned up at that time, still has marked exophthalmos and some tremor. Though I thought her hyperthyroidism was nearly gone, I was distinctly surprised at the normal rate.

As a guide to the amount of roentgen-ray therapy needed in a case of hyperthyroidism due to hyperplasia of the thyroid gland, basal metabolism studies are indispensable and are necessary for scientific work. Case 10 when first seen was a severe type of true hyperthyroidism, and at that time we were not ready to make metabolic rate determinations. We had given her four rounds of roentgen-ray treatments when her first test was made, and in view of her increased weight, slower pulse, great improvement in her nervous condition and her increased strength, together with a rate of only +7 per cent., we discontinued roentgen-ray therapy for one month. By that time her clinical condition was not quite so favorable and her rate had risen to +12 per cent., because of which another round of roentgen ray was given. Case 17 has not been benefited, however, to the same extent, though five complete rounds of heavy therapy have been given. Case 27 had his rate reduced from +58 per cent. to +46 per cent. after two complete rounds of roentgen ray. Case 23, with a rate of +10 per cent. after eleven roentgen-ray exposures, had had marked hyperthyroidism before treatment. Case 36 has had definite clinical improvement and a reduction of rate from +33 per cent. to +21 per cent. after four rounds of roentgen-ray therapy and without absolute rest. Case 55 has had definite amelioration of symptoms and reduction in rate by the use of roentgen ray over several months. In Case 42, however, the condition became steadily worse, operation being contra-indicated with death in a few weeks, though roentgen ray was given in large doses on three different occasions. Our experience indicates a

definite beneficial effect of roentgen ray in cases of true exophthalmic goiter. The amount of therapy necessary to reduce the metabolic rate to normal limits certainly varies with the case. That there is a danger of too much roentgen ray is certain. Moreover, roentgen ray will probably be found ineffective in fulminating cases of the type of Case 42 in our series. With the increasingly low mortality after operative treatment in mind, we cannot at this time recommend roentgen ray as a substitute for surgery in all cases of hyperthyroidism. When it is used the effect must be carefully followed by metabolic rate determinations. This is especially emphasized by an experience of a colleague in another city whose patient remained well for two years after a thyroidectomy. Then he became weak, nervous and his condition suggested a return of his hyperthyroidism and he was sent for roentgen-ray therapy. Soon afterward it was found that he had a −35 per cent. rate and his condition immediately improved on thyroid gland administration. Here roentgen ray was being given where it was absolutely contraindicated and the error was discovered only through metabolic rate studies. All probable cases of mild hyperthyroidism should have their rates determined before roentgen-ray therapy, since many innocent thyroids are undoubtedly frequently roentgen rayed when they should be left entirely alone. By so doing not only will harm be prevented but false cures by the roentgen ray will not be obtained.

Another use of the metabolic test lies in the indication given as to the degree of the toxicity of adenomas of the thyroid. It is well known that adenomatous thyroids may produce no symptoms of hyperthyroidism or that all the symptoms of Graves' disease may occur. Thus the finding of rapid pulse, nervousness and tremor in an individual with an adenoma of the thyroid calls for a determination as to the responsibility of symptoms, whether the gland has taken on excessive secretory activity or whether a neurosis or sympathetic stimulation is causative. Seven cases (2, 11, 19, 24, 45, 67, and 76) with adenomas have been seen, all of which presented some symptoms indicative of at least mild hyperthyroidism. The first two cases had rates of +53 per cent. and +28 per cent., and case 45 had a rate of +74 per cent. The other cases showed normal rates, thus making the percentage of hyperthyroidism in these suspected adenomas only 43 per cent. Case 2, with a rate of +53 per cent. after very extensive roentgen-ray therapy, illustrates the opinion of roentgenologists today that hyperthyroidism due to adenomatous thyroids is not benefited by roentgen-ray treatment in the marked degree that hyperthyroidism due to hyperplasia of the gland is by such treatment. This woman, subjectively, feels a little better but her thyroid is still very active, as shown by her symptoms, and especially by her recent rate of +57 per cent. In spite of an accompanying diabetes and organic heart disease I shall recommend

her for surgery, to be done by local anesthesia. Case 67 had been diagnosticated as having a toxic adenoma, and before a metabolic study was done had received three rounds of roentgen ray with no amelioration of symptoms. The normal rate recently obtained probably indicates that the symptoms for which she was being treated by roentgen ray were neurotic in nature. Case 76 had an intrathoracic adenoma and recently had been told she was extremely toxic, as indicated by a marked tremor and subjective nervousness. Her rate was a normal one, again indicating a functional rather than a toxic nervousness.

As a guide for the surgical removal of hyperplastic, colloid, and adenomatous thyroids, metabolic rate studies have gained recognition from the leading goiter men of the country. Means emphasizes the importance of these tests before surgery, and with Boothby feels that when rates of over +70 per cent. are found, rest or ligation should be resorted to before thyroid removal. During the last two years the goiter surgery of the Mayo Clinic has been directed in a definite way by the results obtained in their metabolic laboratory. Crile is using this test routinely, moreover, in his preoperative studies. It is generally conceded by surgeons, however, that the metabolic rate is not an inflexible guide for surgery, and that even when the rate is high and the clinical condition favorable it is probably safe to operate. It has been suggested that in most cases it would be wise to lower the metabolic rate by roentgen-ray therapy before surgical removal of the thyroid. Indeed in view of the recent article of Means, in which metabolic and clinical studies two years after surgical or roentgen ray treatment showed equally low metabolic rates, with no mortality resulting from the roentgen-ray therapy, we feel that roentgen ray should be kept in mind in the treatment of true hyperthyroidism due to hyperplasia of the thyroid gland before surgery is decided on. As before stated, adenomatous thyroids must be treated surgically, since the metabolic rates are not easily reduced by roentgen ray.

As a method for the diagnosis of hypothyroidism and myxedema, metabolism tests, moreover, hold as an important position as in the diagnosis of hyperthyroid states. Clinicians are always presuming lack of thyroid secretion because of dry skin, thin hair, slow pulse and obesity. Analysis of such cases often shows a perfectly normal rate and indicates that the responsibility of the symptoms cannot be attributed to thyroid activity. Thus in 25 cases recently referred, with the possibility of hypothyroidism, only ten, or 40 per cent., had metabolic rates sufficiently low to indicate too little thyroid or possibly other ductless gland inactivity. Of these 25 cases, 3, 8, 12, 16, 30, 38, 41, 48, 58 and 60 had obesity as their main characteristic and could easily suggest the lack of sufficient thyroid secretion.

CHART I.—BASAL METABOLISM IN ACTUAL AND SUSPECTED HYPERTHYROIDISM.

Case No.	Name.	Date.	Age	Sex.	Ht., in cm.	Wt., in kg.	Av. pulse.	Av. resp.	CO_2 given off c.c.	O_2 absorbed, c.c.	Respiratory quotient.	Cal. per hr.		Metabolic rate, per cent.	Duration of symptoms.	Symptoms, because of which patient was referred for investigation.	Remarks.
												Per kg.	Per sq.m.				
1	G. B.	1920 Mar. 13	29	F	169.57	58.77	130	18	176.5	215.8	0.810	1.05	36.9	− 1.6	7 yrs.	Nervousness; tachycardia	Quiet; drowsy.
2a	E. A.	15	57	F	146.3	50.45	124	20	197.6	267.79	0.730	1.502	53.72	+53.5	2½ yrs. (adenoma of thyroid)	Typical symptoms of hyperthyroidism	Quiet.
2b	E. A.	Aug. 13	57	F	146.3	47.3	120	20	190.2	269.2	0.707	1.590	55.05	+57.2	....	Has had five rounds of *x*-ray treatment	Quiet.
5	M. M.	Mar. 18	25	F	157.0	52.9	120	26	156.2	203.4	0.768	1.094	37.92	+ 1.12	1 yr.	Marked nervousness; slight tremor; loss of weight; tachycardia	Quiet.
6	K. M. R.	18	29	F	153.5	49.8	105	17	139.5	163.5	0.854	0.956	32.68	−12.8	3 yrs.	Marked nervousness; sweating; under weight; slight struma of thyroid	Restless.
7	J. F. J.	April 21	41	F	165.8	44.35	76	13	121.0	176.0	0.688	1.116	33.82	− 6.06	7 mos.	Marked nervousness; sweating; tremor; slight exophthalmos; severe diabetes	Quiet.
10a	A. H.	Mar. 24	28	F	154.5	49.6	118	18	165.4	201.7	0.822	1.177	40.23	+ 7.28	1 yr.	Acute onset of all typical symptoms of hyperthyroidism; has had three *x*-ray treatments, the last being on Feb. 19, 1920, with marked improvement resulting	Quiet.
10b	A. H.	April 22	28	F	154.5	48.65	114	20	163.2	215.0	0.760	1.259	42.2	+12.5	1 mo.	Slight increase in nervousness	Quiet.
11	A. M.	Mar. 24	49	F	161.5	53.2	95	20	209.2	246.2	0.85	1.353	46.15	+28.2	2 yrs.	Tremor and eye signs; adenomatous thyroid of 17 yrs. duration, showing moderate toxic symptoms for 2 years	Quiet.
14	P. C.	27	21	F	160.0	54.55	128	20	227.4	288.2	0.789	1.519	53.15	+41.8	5 mos. (following influenza)	Marked nervousness; tremor; moderate eye signs; tachycardia; sweating	Quiet.
17	Mr. L.	April 2	39	M	166.5	56.6	88	15	246.7	296.5	0.832	1.545	53.2	+31.7	1 yr. (following influenza)	Marked nervousness; moderate eye signs; loss of weight; tremor, weakness	Quiet.
18	E. R.	6	19	F	162.5	49.4	65	18	150.2	179.2	0.839	1.054	34.54	− 9.1	6 mos.	Symmetrical struma; slight nervousness	Quiet.
19	R. E. B.	7	33	F	161.0	52.7	74	16	146.3	174.9	0.837	0.968	32.85	− 6.92	7 yrs.	Moderate nervousness, enlarged thyroid for six to seven years, increased in last year	Quiet.
20	B. H.	8	18	F	164.5	56.62	64	14	142.8	193.9	0.737	0.974	34.4	− 7.4	2 yrs.	Symmetrical struma; slight nervousness	Quiet.
21	M. T.	9	34	F	151.0	46.62	75	15	127.3	163.9	0.777	1.007	33.55	− 4.61	10 mos. (following influenza)	Nervousness; loss of weight; diarrhea	Quiet.

22	G. H.	20	26	F	158.0	62.54	80	14	148.1	185.2	0.80	0.852	32.85	− 9.18	1 yr.	Tachycardia; moderate nervousness; recent tuberculosis	Quiet.
23	M. W.	15	23	F	161.0	48.4	135	15	165.3	211.2	0.784	1.250	40.4	+10.56	1 yr.	Had typical symptoms of hyperthyroidism, which have been diminished by 11 *x*-ray treatments	Quiet.
24	R. B.	14	38	F	170.5	64.3	72	18	193.7	243.4	0.796	0.620	39.99	+15.3	20 yrs.	Large adenomatous thyroid; nervousness; dyspnea; loss of weight	Quiet.
27a	C. N. L.	16	41	M	174.5	60.9	100	14	290.0	366.0	0.793	1.733	60.85	+66.5	8 mos.	Typical symptoms of hyperthyroidism; but able to do light work	Quiet.
27b	C. N. L.	May 18	41	M	174.5	61.6	100	11.5	283.1	337.2	0.84	1.592	56.45	+54.3	....	Has has two *x*-ray treatments, with marked improvement	Quiet; had one dish oatmeal.
31	B. G.	April 21	46	F	164.0	51.15	74	14	140.4	173.0	0.812	0.977	32.45	− 9.88	1 yr.	Marked nervousness; weakness; moderate exophthalmos	Quiet.
32	E. O.	23	19	F	156.0	51.83	92	16	140.9	204.9	0.688	1.133	38.8	+ 2.75	3 yrs.	Nervousness; tachycardia; symmetrical struma of thyroid	Quiet.
33	H. B.	26	34	F	159.0	51.2	79	15	156.2	196.2	0.795	1.103	37.65	+ 3.15	2 yrs.	Recent tuberculosis; nervousness; moderate tachycardia	Quiet.
34	H. S. B.	27	26	F	167.0	57.25	65	12	139.4	193.8	0.720	0.955	33.45	−10.8	1 yr.	Exophthalmos; moderate tremor and nervousness	Quiet.
35	F. B.	29	43	M	160.5	51.6	101	24	233.5	335.5	0.696	1.838	62.1	+61.3	1 yr. (following influenza)	Typical symptoms of hyperthyroidism; able to do light work; condition less severe in last two months	Quiet.
36	D. H. P.	May 1	58	F	158.0	54.45	99	22	183.3	255.0	0.719	1.322	46.6	+33.2	6 mos. (accompanying cholecystitis)	Typical symptoms of hyperthyroidism; has had six *x*-ray treatments	Quiet.
40	B. P.	17	42	F	174.0	52.95	65	12	121.2	157.7	0.769	0.852	27.67	−23.1	2 yrs. (following tonsillect.)	Marked nervousness; weakness; underweight	Quiet.
42	W. H. N.	24	47	F	157.0	53.22	92	17	194.7	248.0	0.786	1.336	46.76	+29.9	6 mos.	All typical symptoms of hyperthyroidism	Quiet.
43	G. F.	26	59	F	163.5	51.6	76	17	120.1	168.4	0.714	0.920	30.8	−12	1 yr.	Nervousness; slight exophthalmos.	Quiet.
45	V. G.	27	35	F	167.0	67.28	130	19	291.5	396.5	0.735	1.667	63.75	+74.6	4 yrs.	Typical symptoms of hyperthyroidism; adenoma	Quiet, very nervous.
47	G. L.	28	31	F	166.5	81.8	85	17	222.6	295.5	0.754	1.027	44.25	+21.2	1 yr.	Marked nervousness; recent tuberculosis; tremor	Very restless.
49	R. R. S.	June 2	32	F	161.0	55.72	71	14	139.3	179.2	0.778	0.922	32.46	−11.0	3 yrs.	Nervousness; long-continued mild temperature	Quiet.
50	T. C.	4	40	F	161.0	55.45	74	8	156.0	191.4	0.816	0.996	35.04	+ 2.6	6 mos.	Marked nervousness; tremor	Quiet.
51	F. E. B.	5	58	F	164.0	45.25	108	18	168.8	215.7	0.784	1.366	42.30	+20.9	8 mos.	Typical symptoms of hyperthyroidism	Quiet.
53	R. J. C.	9	24	M	168.5	58.7	92	10	202.8	256.0	0.793	1.252	44.05	+11.5	1 yr.	Nervousness; tremulousness; tachycardia	Quiet.
54	M. C. S.	11	48	F	159.0	61.55	115	19	216.8	274.0	0.792	1.278	48.45	+34.6	5 mos.	Moderate exophthalmos, tremor and nervousness; slightly enlarged thyroid	Quiet.

CHART I—CONTINUED.

Case No.	Name.	Date.	Age	Sex.	Ht., in cm.	Wt., in kg.	Av. pulse.	Av. resp.	CO_2 given off c.c.	O_2 absorbed, c.c.	Respiratory quotient.	Cal. per hr.		Metabolic rate, per cent.	Duration of symptoms.	Symptoms, because of which patient was referred for investigation.	Remarks.
												Per kg.	Per sq.m.				
		1920															
55	E. T.	June 12	23	F	173.0	58.7	118	20	228.3	286.0	0.799	1.403	48.47	+27.0	2 yrs.	Marked exophthalmos, nervousness; tachycardia and loss in weight; has had 7 *x*-ray treatments	Quiet.
56	P. A. E.	14	41	F	168.5	91.1	122	40	503.0	562.0	0.895	1.816	82.3	+128.6	1 yr.	Very marked nervousness, tremor, sweating and weakness; slight exophthalmos; loss of 60 pounds; marked dyspnea; enlarged thyroid; tachycardia; impossible to rise from a sitting posture	Quiet.
61	E. A.	29	20	F	166.8	49.4	79	20	137.5	202.6	0.680	1.152	37.2	− 0.8	2 yrs.	Small struma; tachycardia; loss of weight	Quiet.
62	N. C.	29	51	F	162.0	76.45	64	15	165.2	216.0	0.765	0.806	34.03	− 2.27	4 yrs.	Marked nervousness; weakness; dizziness	Quiet.
63	H. H. A.	July 9	23	F	161.0	66.6	86	8	146.2	238.7	0.613	1.038	40.72	+ 8.6	1 yr.	Has had skin eruption; thought by dermatologist to be due to thyroid disturbance	Quiet.
65	C. S.	10	42	M	175.0	67.3	50	8	179.3	273.1	0.662	1.142	40.7	+13.05	1 yr.	Tachycardia; sweating; nervousness	Quiet.
67	L. B.	31	26	F	158.5	48.02	86	19	148.7	193.7	0.769	1.154	37.7	+ 0.53	4 yrs.	Marked nervousness; slight tremor; small adenoma; has had right lobe of thyroid removed	Quiet.
68	E. H.	29	53	F	152.0	61.35	70	13	147.7	206.8	0.715	0.948	36.98	+ 5.66	1 yr.	Nervousness; increased perspiration	Quiet.
72	M. M.	Aug. 12	38	F	165.5	79.1	85	17	166.3	234.7	0.709	0.835	35.2	− 3.56	2 yrs.	Nervousness; tachycardia; loss of weight	Quiet.
73	L. McC.	16	42	F	152.25	51.55	73	18	139.8	194.6	0.718	1.066	37.61	+ 4.48	1 yr.	Nervousness; slight tremor	Quiet.
75	D. B.	28	19	F	161.0	47.3	86	15	116.7	181.5	0.707	1.108	35.75	− 5.94	4 yrs.	Marked nervousness	Drowsy; quiet.
76	M. R. W.	26	58	F	164.0	59.7	84	15	146.0	210.0	0.696	0.991	35.8	+ 2.9	25 yrs.	Intrathoracic adenoma of 25 years' duration; recent nervousness, tachycardia and weakness	Quiet.
77	W. H. O.	31	22	F	164.5	65.9	53	16	152.3	213.3	0.715	0.909	34.88	− 7.0	1 yr.	Marked nervousness; emotional instability	Quiet.
79	N. H.	Sept. 4	36	F	162.5	56.4	68	16	162.3	224.9	0.723	1.125	39.8	+ 9.0	1 yr.	Colloid goiter; weakness; marked nervousness	Quiet.
80	H. McQ.	7	26	F	162.0	51.85	76	11	117.8	193.2	0.707	1.047	35.64	− 4.96	4 mos.	Nervousness; slight struma, gradually reducing since tonsillectomy one month ago	Quiet.

None of them showed too low rates. Cases 64, 66 and 78 had been taking thyroid just before the metabolic rate was determined. The slightly increased rates might indicate the ordinary response of a normal individual to thyroid medication, and to be sure these cases are hypothyroid in type, the rates should be determined again two or three weeks after the cessation of thyroid administration. Case 59 when first seen one year ago was a typical advanced case of myxedema with anemia, non-pitting edema and mental disturbances. At present she is taking thyroid very intermittently and feels well, though her rate is still −28 per cent. Case 48 is one of obesity with a collar of abnormal fatty deposits around the neck. His rate of +18 per cent. indicates no lack of thyroid secretion. He eats moderately and perspires freely, but still maintains his excessive fat in spite of his rather high rate.

Finally, as a guide to correct thyroid administration, metabolic rate determinations are of the greatest value. As already stated, hypothyroidism with consequent thyroid therapy is undoubtedly often misdiagnosed. Metabolic studies, moreover, as pointed out by Means, usually show it takes much less thyroid to keep that rate at normal than is often given, and equally important it is found that the rate can be elevated considerably above normal for some time without producing symptoms of hyperthyroidism. That such therapy does harm, moreover, even when symptoms are not present, is shown by a case recently seen in which thyroid administration in rather large dose for obesity suddenly produced a dilated thyrotoxic heart. This emphasizes the necessity of the use of the metabolic rate studies as a means of first being sure of your clinical diagnosis and second of gauging the amount of thyroid therapy. At present in the use of the dry thyroid gland we have little idea of the strength of the preparation. Kendall has shown that the amount of thyroxin in thyroids varies according to seasons. The active principle of the thyroid which Kendall recently has isolated in pure crystalline form will probably soon be used by many physicians for accurate thyroid administration. Plummer has shown that 1 mg. of this thyroxin raises the metabolic rate about 2 per cent. and that it takes about 1 mg. a day to keep the rate of a myxedematous patient up to the normal. However, he determines this dose by metabolic rate studies. The effect of administering desiccated thyroid gland is shown in Case 4, in which the rate was raised in one month from −13 per cent. to +7 per cent. by a dose of 1 grain twice daily. Possibly this dose, for this woman of good size, will, if continued, raise her rate above normal; but this can best be determined by other tests. We feel that thyroid administration to children should be guided, if possible, by metabolic studies, and that these studies should be the basis for the diagnosis of mild hypothyroid states that are so often assumed by clinicians in their young patients. No child should receive thyroid simply because he looks "a little hypothyroid in type."

CHART II.—BASAL METABOLISM IN ACTUAL AND SUSPECTED HYPERTHYROIDISM.

Case No.	Name.	Date.	Age	Sex.	Ht., in cm.	Wt., in kg.	Av. pulse.	Av. resp.	CO_2 given off c.c.	O_2 absorbed, c.c.	Respiratory quotient.	Cal. per hr.		Metabolic rate, per cent.	Duration of symptoms.	Symptoms, because of which patient was referred for investigation.	Remarks.
												Per kg.	Per sq.m.				
	1920																
3	J. E. L.	Mar. 17	40	F	167.5	103.8	90	14	232.0	284.2	0.817	0.792	38.79	+ 7.75	38 yrs.	Over weight	Quiet.
4a	A. K.	18	37	F	155.5	68.55	79	21	147.1	181.4	0.812	0.784	37.5	−13.7	6 mos. (following encephalitis lethargica)	Increased weight; apathy, weakness; moderate exophthalmos	Quiet.
4b	A. K.	May 3	37	F	155.5	68.55	79	21	172.2	231.5	0.744	0.96	39.12	+ 7.18	....	Has taken 1 gr. of desiccated thyroid twice daily for one month	Quiet.
8	J. S. R.	April 12	57	F	158.0	72.0	65	18	153.0	185.2	0.832	0.707	30.72	−12.2	5 yrs.	Obesity; sluggish mentality; thin hair	Quiet; sm. breakfast.
12	M. S.	Mar. 25	79	F	164.4	81.8	58	16	164.1	195.3	0.841	0.694	30.12	− 8.7	2 yrs.	Dry skin; falling hair; slight mental dulness; no increase in weight	Quiet.
16	R. B.	April 1	31	F	172.0	98.9	64	11	200.6	252.8	0.794	0.735	34.42	− 5.7	4 yrs.	Obesity; dry, inactive skin; thin hair	Quiet.
26	F. R.	15	26	F	163.5	68.4	84	14	196.1	231.8	0.846	0.986	38.44	+ 2.5	4 mos.	Slight increase in weight; pregnancy, with some suggestions of hypothyroidism	Quiet.
28	Mrs. M.	19	48	F	164.5	54.3	78	10	132.7	171.9	0.772	0.907	30.95	−14.0	20 yrs.	Secondary anemia; relative lymphocytosis; myxedematous facies	Quiet.
30	L. Y.	20	19	F	161.5	69.35	66	18	176.9	224.3	0.789	0.929	37.05	− 2.5	3 yrs.	Obesity; inactive skin	Quiet.
37	E. E. M.	May 7	59	F	161.0	75.8	71	17	131.8	194.6	0.678	0.721	30.38	−13.2	4 yrs.	Nervousness; obesity; dyspnea	Quiet.
38	H. J. K.	12	31	F	160.5	96.77	72	17	204.8	283.6	0.723	0.827	40.01	+ 9.62	8 yrs.	Obesity; inactive skin	Quiet.

39	J. A.	15	19	F	175.0	96.45	63	12	167.3	243.6	0.688	0.711	32.27	−15.1	4 yrs.	Obesity; apathy; slow pulse; thin hair	Quiet.
41	L. C. C.	22	52	F	162.0	89.15	68	16	155.4	225.0	0.692	0.710	32.55	− 7.0	20 yrs.	Obesity; lack of perspiration; thin hair	Quiet.
44	R. E. D.	June 2	36	F	169.5	95.3	64	15	176.2	239.4	0.742	0.710	32.68	−10.45	2 yrs.	Obesity; apathy; dry skin	Quiet.
48	M. T. C.	Aug. 12	48	M	162.75	77.3	73	15	216.5	296.5	0.730	1.083	45.77	+18.87	8 yrs.	Obesity; abnormal fat pads over shoulders	Quiet.
52	Mrs. C.	June 9	38	F	161.5	70.55	60	19	150.7	202.3	0.745	0.814	32.75	−10.27	4 yrs.	Had typical symptoms of hypothyroidism and has been greatly benefited by thyroid administration	Quiet.
58	S. A. M.	24	54	F	162.5	65.6	74	14	151.6	210.4	0.721	0.905	34.73	− 0.77	3 yrs.	Weakness; falling hair; general hypothyroid appearance	Quiet.
59	T. W. H.	24	55	F	164.0	56.4	54	12	101.2	143.0	0.708	0.712	25.12	−28.2	4 yrs.	Typical symptoms of myxedema; has taken thyroid intermittently for last year with great improvement	Quiet.
60	J. T. W.	28	72	F	162.5	76.55	63	16	154.1	216.5	0.713	0.796	33.48	+ 1.45	8 yrs.	Obesity; thin hair; apathy	Quiet.
64	L. H.	July 1	32	F	150.5	67.3	85	18	175.0	249.3	0.703	1.042	43.0	+17.8	2 yrs.	Has been taking thyroid for one year with marked improvement; 10 pounds loss in weight	Quiet.
66	E. A.	Aug. 6	52	F	165.5	83.72	64	16	188.4	249.4	0.756	0.855	37.15	+ 7.7	2 yrs.	Large and heavy; puffy facies; rather thin hair; active skin; slight nervousness	Quiet.
69	L. L.	2	42	F	154.0	66.65	67	13	133.8	173.4	0.772	0.745	30.07	−16.48	3 yrs.	Generalized non-pitting edema; thin hair; increased weight; apathy	Quiet.
71	G. K.	10	29	F	169.0	95.1	66	9	169.8	220.4	0.771	0.662	30.45	−18.8	3 yrs.	Obesity; apathy; dry skin; has taken 5 gr. thyroid daily for one month with great improvement	Quiet.
74	F. D. L.	25	51	F	167.0	63.45	46	11	113.3	166.3	0.688	0.738	27.23	−22.2	2 yrs.	Non-pitting edema; slight apathy	Quiet.
78	I. S.	Sept. 1	45	F	152.5	67.3	72	16	188.4	240.0	0.786	1.022	41.72	+15.9	30 yrs.	Overweight; dry skin; has been taking thyroid	Quiet.

Conclusions. The *importance* of basal metabolism studies in the handling of thyroid diseases must be recognized. By metabolic rate determinations we are greatly aided in our diagnosis of early and obscure cases of hyperthyroidism. Moreover the degree of severity of an obvious hyperthyroidism can be determined by this test. Again the presence or absence of toxicity of an adenomatous thyroid is made evident through these metabolic studies. As a guide for surgical removal of goiters, surgeons are recognizing the value of this test. Finally in the diagnosis of hypothyroidism and in directing and gauging thyroid administration metabolic rate determinations are of the greatest importance.

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BLOOD CHANGES IN A GASTRECTOMIZED PATIENT SIMULATING THOSE IN PERNICIOUS ANEMIA.

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Gastrectomy is a term often applied to an operation which is merely a resection of the major portion of the stomach. This statement coincides with Sir Berkeley Moynihan's opinion, who reviewed the history of gastrectomy in 1907 and added to the literature two cases of his own, bringing the number of reported cases to seventeen. Three doubtful cases are included in his series. Moynihan states that the first complete gastrectomy was performed by Conner in 1883. The patient died on the table. The next complete resection for carcinoma was performed by Schlatter in 1897. The patient lived fourteen months and died because of a recurrence. Moynihan's patient lived the longest after operation, three years and eight months.

My attention was first called to cases of this type by a man (Case 204441) who presented himself at the Clinic for examination on August 10, 1917. The patient was fifty-eight years of age. He had complained intermittently for the past fifteen or twenty years. His illness was characterized by exacerbations of months' duration and by a dull, heavy pain in the epigastrium immediately after meals. The pain subsided from three to four hours after meals and a sensation developed which the patient described as a hunger more distressing than the immediate after-meal pain; this was relieved by food or drink. A clinical diagnosis was made of peptic ulcer. Malignancy was suspected because of recent continued gastric distress, recent loss of fifteen pounds in weight and rapid decline in strength in the past four months.

The blood-pressure was normal. The hemoglobin was 80, erythrocytes 5,520,000 and leukocytes 8200; the index was 0.7+. No differential count was made. A single tubing of the stomach revealed 120 c.c. of gastric contents in one and one-half hours after a modified Ewald meal. No free hydrochloric acid was found; the total acidity was 4. The roentgenologist reported an indeterminate pyloric lesion. After careful dental examination four teeth were condemned because of apical abscesses and two were held under suspicion. The examination otherwise was of no special importance. The patient was operated on August 18, 1917 (W. J. Mayo). The dictated description of the operation reads as follows:

Operation. "A median incision was made which extended well up to the ensiform cartilage. A movable carcinomatous ulcer was found on the posterior wall of the stomach extending up to within almost 4 cm. of the esophagus. A total gastrectomy was performed

and about 1 cm. of the esophagus removed. The end of the esophagus was sutured to the lateral wall of the jejunum, about 45 cm. from its origin, with interrupted silk and continuous catgut. The line between the esophagus and cardia was visible and was removed. Fat and glands were removed up to the diaphragm. There was very little glandular involvement." The pathological report from tissue removed was "carcinoma of the cardiac end of the stomach with no glandular involvement." Specimen showed the transition of esophageal tissue into the gastric tissue and of gastric tissue into the duodenal tissue. This is interesting from an operative point of view.

The patient returned to the Clinic on June 29, 1918. He had been comparatively well after the operation but had lost seven pounds in weight. He complained of epigastric pain, heart-burn, a heavy

FIG. 1.—Case 204441. Photomicrograph, showing transition of the esophageal mucosa into the gastric mucosa.

sensation and excessive salivation after meals. He was, however, taking three fair-sized meals each day with a glass of milk between meals. The bowel movements were loose, one to three stools each day. The scar of the operation had healed by first intention. Palpation of the abdomen revealed no pathological condition. Because of the patient's apparently favorable condition, with the exception of his weight, no laboratory tests were made.

May 5, 1919, the patient again visited the Clinic. He had grown progressively weaker during the last year, more rapidly the last three months. His diet was general and fairly well balanced. He complained of regurgitation after meals which, if long continued, resulted in the regurgitation of bile; this was fairly well controlled

by salt-water, a prescription of his own. He was somewhat paler than on the previous examination, and his wife stated that he was "more yellow" at times. He weighed 100 pounds. There were no paresthesias or lightning pains; the mouth had not been sore; the mucous membrane of the tongue was somewhat smooth at the edges. The most interesting feature was disclosed by the laboratory study of the case, particularly of the blood. The urine showed a faint trace of sugar, even on a starch-free diet; it contained a faint trace of albumin, a few hyaline casts and pus cells and was slightly acid in reaction; the specific gravity ranged between 1012 and 1018.

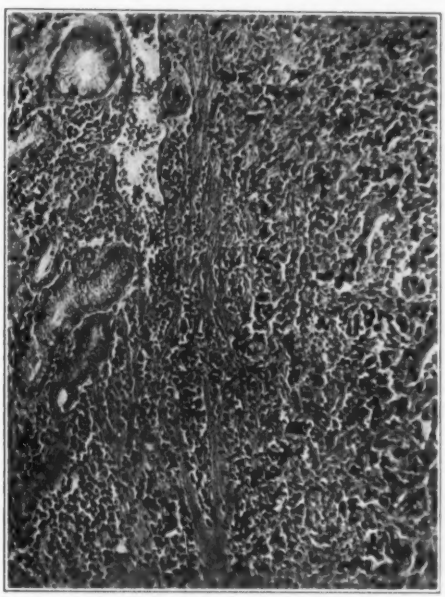

FIG. 2.—Case 204441. Gastric carcinoma at the base of the ulcerated area.

The blood sugar by the Benedict method was 0.05 per cent. The patient declined further study of the nature of the glycosuria. The cytologic study of the blood revealed the picture of pernicious anemia. The hemoglobin ranged between 53 and 55; the erythrocytes were between 2,000,000 and 2,280,000; the white cells varied between 2200 and 7600, and the color index was constant at 1.2+. The differential count read as follows: 200 cells counted; polymorphonuclear neutrophils, 59 per cent.; small lymphocytes, 35.5 per cent., large lymphocytes, 5.5 per cent. Slight anisocytosis and poikilocytosis were present. The Ribiere test revealed an increased resistance of the red cells. The blood Wassermann test was negative.

The blood was classed in Group IV. An analysis of the duodenal content estimated in Wilbur and Addis units showed an increase in bilirubin, urobilin and urobilinogen. A neurological examination did not reveal cord changes or other abnormalities. The pancreatic ferment test showed marked reduction of pancreatic activity. Roentgenograms of the chest and the esophageal-jejunal juncture were negative. In consultation it was decided that although the blood count was that of pernicious anemia several clinical features of pernicious anemia were lacking.

While it is realized that the study of one case is of no value in drawing conclusions, it may nevertheless give a possible clue to the cause of pernicious anemia. The case under discussion suggests that the absolute lack of gastric ferments might have something to do with an incomplete or abnormal food-splitting process, the results of which might themselves be hemolytic to the blood or detrimental to the blood-forming organs. Pernicious anemia is invariably associated with achylia. This patient was, of course, completely deprived of gastric juice by the operation, and in the course of time returned to the Clinic with a blood picture of pernicious anemia. Immediately the question arises—Why do not all patients with achylia develop pernicious anemia? a question which cannot at present be answered.

With this theory of the cause of pernicious anemia in mind a thorough review of the French, Italian, German and English literature was undertaken. Much has been written on the operative technic and the immediate postoperative results of complete gastrectomy but with one exception, Moynihan's second case, no report was found in which a patient's subsequent history had been followed for any length of time. Moynihan's patient was a man, aged forty-three years, who had a two-year history of delayed gastric distress one hour after the ingestion of food. The pain was relieved for about one hour by food and by vomiting, which was obstructive at the time of examination. The patient also complained of a dysphagia. May 31, 1907, a complete gastrectomy was performed for carcinoma of the stomach, situated high on the lesser curvature. The esophagus was sutured to the first jejunal loop by interrupted and continued sutures. The patient's immediate postoperative convalescence was rapid and satisfactory and he left the hospital in eighteen days. Moynihan again discussed this case in 1911, stating that the patient had been in normal health until 1910, when "he began to show evidences of profound anemia and was strikingly pale and breathless, and he lost weight." He improved under treatment so that he was able to return to the work he had done formerly. In August, 1910, he again failed in strength, although his appetite was good and he had no indigestion. In October the anemia reappeared and he was obliged to stop work. In the latter part of December the patient was confined to bed; he died January

31, 1911, having survived the operation three years and eight months. The following is the summary from the necropsy report by Goffery Steward: "All the organs exhibited an extreme anemia; the blood in the heart and great vessels was watery. The liver was pale and somewhat fatty. The spleen contained a large and very old infarct. The heart muscle was pale and flabby. No recurrence of the carcinoma was found. The chief points of interest were, (1) the complete absence of any recurrence or dissemination of the malignancy; (2) the profound anemia, and (3) the absence of any striking jejunal dilatation at or near the site of anastomosis."

In Moynihan's case, as in the one herewith reported, there were recurring anemia and weakness, with some of the pathological changes seen in pernicious anemia. Apparently pernicious anemia was not thought of in this case; otherwise a more complete necropsy report would have been made, together with reference to the pathology of the bone-marrow. However the history is suggestive of pernicious anemia and adds its bit to the evidence at hand.

June 1, 1920, our patient returned to the Clinic in a somewhat weaker condition. The recrudescences and remissions of his anemia were of shorter duration than are usually observed in pernicious anemia, while his health in general was in a steady decline.

The patient had had six severe attacks of abdominal pain lasting from one-half hour to five hours; they were sudden in onset, were associated with the vomiting of large quantities of bile and were terminated by the results of a purge. They were not accompanied with jaundice. Urinary symptoms were absent with the exception of slight frequency. The diet was liberal; the patient ate fish, liver, pork, cabbage, eggs, milk, potatoes, squash, carrots, lettuce, radishes, sauces, jellies, candies, fruits, peanuts, toast, waffles and so forth. Practically the only foods which distressed him were meat, which he craved, and fresh bread. These seemed to precipitate regurgitation. The general course of the anemia seemed to be a steady decline with short recrudescences and remissions rather than of marked remissions. The examination of the eyes, including the fundi, was negative. There was no glossitis and the atrophy at the edge of the tongue had not spread. The abdomen was pasty but nothing abnormal was palpable. There was moderate edema of the legs as far as the knees. The systolic blood-pressure was 120 and the diastolic was 80. The pulse-rate was 78. The specific gravity of the urine was 1016; it was slightly alkaline and, aside from a trace of albumin, was negative. The hemoglobin remained quite constantly at 48 per cent. and the erythrocytes varied between 1,420,000 and 1,880,000, the leukocytes between 4000 and 4700 and the color index between 1.2+ and 1.6+. The differential count showed polymorphonuclear neutrophils 64 per cent., small lymphocytes 33 per cent. and large lymphocytes 3 per cent. Anisocytosis was moderate, poikilocytosis and poly-

chromatophilia were slight. The platelet count was 126,000. The blood Wassermann test was again negative. The coagulation time (Lee method) and calcium time were eight minutes. There was an increased resistance of the red cells. A roentgen ray of the chest and of the esophageal-jejunal juncture was negative. The pancreatic test of the stool was less than 250 units (Wohlgemuth test). Schmidt's test of the stool for bile was positive. The stool was thick and white, containing undigested meat fibers, mucus and fat, but no parasites. The blood picture was again considered suggestive of pernicious anemia, but with several unusual features.

It is emphasized that no attempt has been made to drawn conclusions from these two cases; they do, however, open a field for investigation. Dr. Mann, of the Mayo Foundation now has begun as experimental study of the blood changes following gastrectomy.

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STREPTOCOCCUS HEMOLYTICUS EMPYEMA.[1]

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Since February of this present year we have been much impressed by the frequency of pleural effusions. During the pandemic of influenza of 1918 this feature in our experience was very infrequent, but common in this outbreak. Among our cases there were over 25 which could be classified as empyemata; 7 of these were due to the streptococcus hemolyticus. These 7 patients developed this feature as a complication and not a sequel of acute pulmonary infection; they were treated by frequent aspirations, which was followed by subsequent resection; the number of aspirations aver-

[1] The material upon which this article is based was presented at the monthly conference of the staff of the Mercy Hospital. The article itself was prepared for the Pennsylvania Section, Clinical Congress of the American College of Surgeons, at Pittsburgh, October 7, 8, 9, 1920.

aged seven in number; the length of time between aspirations was two or three days; the period before resection was done was between two and three weeks; no washing of the pleuræ was practised and all recovered, but over a prolonged period of time. Two of these cases required second resection despite the proper surgical procedure skilfully carried out.

Moschcowitz, in the Mütter Lecture of 1919, has written extensively on empyema, and from a surgical as well as from a pathologic aspect has done much to bring this old subject to a better understanding. One hesitates after the recent articles by Witenskey, Behrend and others to approach the subject, but the analysis of our work from the internist point of view during these few months has been instructive to us and is the basis upon which this brief record is presented. Before entering upon the consideration of this group, cognizance of certain general ideas seem pertinent. A limited questionnaire presented to certain surgeons among our colleagues upon the subject of empyemata and their results almost uniformly elicited the response that empyema was a simple surgical procedure, and the results of operations were uniformly good. This attitude of the surgeons which has long prevailed seems to us will have to be changed, particularly in dealing with those empyemata which are due to the Streptococcus hemolyticus. The results of former surgical practice in the early part of the war gave the army surgeons such a startling mortality as to compel them to reconsider the methods of dealing with empyemata. The diagnosis of pleural effusion, its pathology and end-results in Streptococcus hemolyticus empyema are of importance and worthy of the greatest concern both from the point of a life-saving procedure as well as for a problem of functional restoration to health. This type of empyema seems now to us, and probably to all surgeons, a different surgical problem from the empyemata due to the other causes. The entity may and probably will disappear in a short time from among our clinical work, but its significance at the present time must be appreciated, and we believe met by certain methods now well known and advised by internists and surgeons of wide opportunity. Again a certain idea must be emphasized, neglect of which makes the results in these cases hazardous, and that is that this is a complication of pneumonia rather than a sequel. While a result of pneumonia always, nevertheless it is an immediate complication, and as such must be met in a different way from other forms. Our work makes us believe, and this is in accord with others, that the effusion is a purulent one from the start and not an effusion, at least not in bulk, subsequently infected. While with the opinion expressed by certain writers that some of these empyemata are cured by simple aspirations, we are not in accord, nor are we in harmony, with delayed treatment. This simple fact of complication rather than sequel should be borne in mind, and we do not feel that it can be over-

emphasized, for it is this conviction upon which the recent methods of treatment and good results are based. The appreciation of the formation of the empyema from pneumonia admirably explained by Moschcowitz and others is acceptable and explains the pathology.

This complication comes on so rapidly and early, a fact recorded by others, that after a few failures of early recognitions we grew to suspect its frequency, and its recognition was subsequently rarely at fault. The patients were so ill that physical signs and exploration were depended upon, the fluoroscope studies being postponed until the case became one of surgical sequel rather than complicated pneumonia. The sign of increased, high-pitched, vocal resonance helped us more than any other sign in finding fluid present even when the amount was small. These patients improved at once after the first aspiration which seemed out of proportion to the amount of fluid withdrawn. The mechanical factor of cardiac displacement seemed of less importance than the presence of toxic effusions. The first aspiration showed the Streptococcus hemolyticus, and all subsequent aspirations were consistent from a bacteriologic study up to the time of resection. The number of aspirations averaged from five to seven, extending over a period of two weeks or more, when from a patient with a very high surgical risk the case became one for good surgical work and was considered safe from a prognostic point of view. Elliott also, with rather full plate work on the thoraces of his cases, stated that the number of aspirations on his patients were four or five and the length of time involved a period of two weeks. Our own more frequent aspirations and greater length of time seemed to us better, although, too, late resection has one drawback to which we find brief reference by others and which we encountered in three of our patients, namely, dense pleural adhesions. The character of the fluid withdrawn grossly inspected was a feature which attracted our attention and has been spoken of by others. The first fluid taken when the patient was in the midst of his infection or earlier was of an amber color, but not the clear, serous fluid of exudate usually encountered. By the time the second or third aspiration was performed the pus was frank and the later ones were of the same character but denser in quality. After five or six aspirations the pus assumed a chocolate appearance, and to us this appearance indicated the time for resection. At this time the clinical picture of the patient was that of convalescence from acute infection. This feature of sequence in the appearance of the pus was very constant, and we think is worthy of note, and has been so stated by others. With the opinion that the chocolate appearance of the pus is due to the traumata of frequent aspirations as suggested by one surgeon we cannot entirely concur. The day previous to the removing of the patient to the operating room the final aspiration was done. A very striking and consistent feature was the large amount of fluid sometimes withdrawn. In one instance

we withdraw about 3 liters from a large man during his second aspiration, when 1½ liters had been withdrawn only a few days before. Such large amounts can easily be dangerous to life, because of the now known although not generally appreciated elasticity of the mediastinum which produces interference with the other side of the thorax.

We have practised preliminary tapping in all forms of empyemata at Mercy Hospital for many years, when cases were not too urgent, and believe strongly in it.

The problem of washing the pleural cavity after the resection and insertion of the tubes is worthy of great consideration, and we believe this may be the better plan, judging from the experience of other men, and shall consider it in the future should such cases come under our care. One case of a colleague not in this group did well under the Carrel-Dakin solution. This may shorten the time of cure.

Our own feeling was for costatectomy instead of thoracotomy, and this we had performed. Many other men are in favor of the latter and with a simpler procedure and earlier washing with the Carrel-Dakin solution this may suffice for cure in some cases. The fact that two of our patients required second resection to establish sufficient drainage, although well done at the primary operation, makes us in favor of the former at present.

There were 2 cases in this group of dense adhesions which presented a problem difficult of solution and are yet unsolved. The 7 cases due entirely to the Streptococcus hemolyticus treated as we have outlined, and with no deaths, seems to warrant this record. The disappointments were the long periods of convalescence and the dense adhesions which followed in 2 of the cases. The use of the Carrel-Dakin solution in the future may remove such disappointments.

INTERNAL HYDROCEPHALUS IN A SYPHILITIC, PROBABLY DUE TO INTRASPINAL TREATMENT.

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and

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The common dangers of the intraspinal treatment of neurosyphilis have been discussed by various writers and are now generally known. Among the most important are septic meningitis, due to faulty technic; death from respiratory paralysis; paraplegia; loss of bladder and rectal sphincter control; sensory changes about the

perineum and in the legs. So far as we have been able to determine, internal hydrocephalus has not been mentioned in this connection. We therefore wish to record a case presenting this interesting but distressing complication.

History. The patient is a young white man, an attorney by profession, aged thirty-two years. He has been married for five years, but there have been no pregnancies.

In 1907 he contracted a genital sore, which was painful, with a seropurulent discharge but no local adenopathy. The sore persisted for six months. One month after its appearance he developed a sore throat, followed in another month by rheumatic pains and by small sores in the mouth. Three months later a generalized macular rash, together with lesions at the anus, appeared. Treatment consisted of "powder" by mouth.

In 1912 he began to suffer with occasional mild headaches, worse in the late afternoon and night, and with shooting pains in the legs. The headaches persisted with increasing severity until 1915, when they became severe enough to cause him to consult a physician. The blood Wassermann at that time was positive. One intravenous injection, presumably arsphenamin, followed by a course of intramuscular mercury and potassium iodide, brought about a decided improvement.

During the next three years he developed loss of libido and potentia, girdle sensation, difficulty in mental concentration and a change in disposition manifested by heavy drinking. The headache did not recur until about July, 1918, and was then of only slight intensity; it followed his rejection by an Army Medical Examining Board because of a diagnosis of "cerebrospinal syphilis." He was told at this time that the Wassermann of the blood and spinal fluid were both positive, whereupon he placed himself under treatment, consisting of six intravenous injections of arsphenamin and one intraspinal injection of mercurialized serum. Following this the blood Wassermann was said to have become negative.

Several hours after the intraspinal treatment there was a severe reaction, consisting of excruciating headache and pains in the legs lasting for four days, during which time he remained in the hospital. When he went home on the fifth day he felt fairly well, but on the sixth day he was suddenly seized with a fresh, terrific headache and pains in the legs. For the next forty-eight hours he was said to have been delirious and to have had a high temperature. He had stiffness of the extremities and retraction of the head. With this late reaction he remained in bed ten days.

For the next six weeks he felt quite well, but gradually an entirely new sort of headache began. The old headache had been infrequent, mild and generalized. These new headaches were almost constant, occipital and of terrific intensity. To quote his own expression, he "nearly went crazy with the pain." On two occasions during this phase of his condition he attempted suicide.

Physical Status. In December, 1918, he consulted one of us. At that time the physical examination showed round, regular pupils of the Argyll-Robertson type, coarse tremor of the tongue, pain on pressure over the cervical spine, absent knee- and ankle-jerks and oral sepsis. Psychiatric examination showed none of the characteristic signs of general paralysis.

Serology. The blood Wassermann was negative; the cerebrospinal fluid examination showed fifty cells, a strongly positive globulin test, Wassermann positive with 0.1 c.c. and a paretic type gold curve.

Treatment. When first seen his headaches were thought to be due to cerebrospinal syphilis, and from December 23, 1918, until October, 1919, he was kept under continuous antisyphilitic treatment. During this time he received seven intraspinal injections of mercurialized serum according to a method described by us,[1] six spinal drainages followed by arsphenamin and eleven separate intravenous injections of arsphenamin products, a total of twenty-four intravenous arsphenamins. From the standpoint of serology the results obtained were gratifying. The blood Wassermann remained negative and on October 14, 1918, the cerebrospinal fluid showed six cells, a slightly positive globulin, Wassermann negative with 1.0 c.c. and a negative gold curve.

Progress. Clinically, however, it was noted that the patient improved but little. Reactions following the intraspinal treatments were exceptionally severe, consisting of unbearable headache and pains in the legs, rendering a continuation of intraspinal medication impossible.

From December, 1918, until July, 1919, the headache continued almost as severe as before. During the next three months, however, a very considerable improvement took place; but after an intraspinal treatment on November 3 the pain recurred and rapidly grew worse until, during December, headache was constant, sometimes requiring morphin for relief.

November 29, examination of the eye-grounds disclosed unilateral choked disk right, with some edema of the left disk, and a high degree of vascular sclerosis. Consultation with an ophthalmologist revealed in addition marked compound hypermetropic astigmatism. With the hope that the edema of the disk would subside spontaneously and that the refraction error might, at least partially, account for the headache the error was corrected with glasses, but without relief.

In reviewing the patient's course at this time we found as evidence of increased intracranial pressure the severe headache and the low-grade choked disks, but no nausea, vomiting, bradycardia or localizing symptoms. It was recalled that from May 2 until

[1] Keidel, A., and Moore, J. E.: Treatment of Neurosyphilis by the Intraspinal Route, Johns Hopkins Hosp. Bull., November, 1920, xxxiv, 404.

October 4 treatment had been intravenous only, no lumbar punctures having been done. October 4, 11, 25 and November 3 spinal drainage was carried out. On the first date (October 4) the pressure was markedly increased and the fluid spurted out in a steady stream to a distance of several inches. When 70 c.c. had been rapidly removed the procedure was terminated for fear of reducing the intracranial pressure too quickly. At the four succeeding drainages it was noted that the pressure seemed to grow progressively lower, so that at the time of the last treatment, on November 3, spinal fluid flowed only drop by drop, and ceased to flow at all after 40 c.c. had been obtained.

Laryngological consultation on September 20 had been completely negative for any sinus disease, either of the frontals, antra, sphenoids or ethmoids.

It being by this time obvious that we were dealing with some intracranial condition, careful review of the various symptoms just outlined prompted the suspicion of an internal hydrocephalus, perhaps due to an old meningitis, with adhesions in the floor of the fourth ventricle.

Stereoscopic Roentgenologic Examination of the Head on December 29 showed the following rather startling picture: "The parietal sutures on both sides, especially near the top of the head, are distinctly separated. The lambdoidal sutures are also very decidedly separated. The sella turcica is quite large, but this may be a normal variation. There are no shadows to indicate a localized tumor in any place. There is no evidence of a periostitis to indicate lues. The condition suggested an intracranial pressure affair without being able to pick out the particular lesion. The paranasal sinuses show an absence of both frontals. The maxillary sinuses are small but clear."

Surgical Consultation. This lent added weight to our tentative diagnosis. December 31, 1919, Dr. George Heuer saw the patient in consultation and confirmed the presence of bilateral choked disk, more marked on the right. There was also a questionable bitemporal hemianopsia. Right subtemporal decompression was decided upon and was performed January 24, 1920. At operation very troublesome bleeding was encountered from the posterior branch of the middle meningeal artery as well as from the other dural vessels, all of which were much larger than normal. The dura was under slightly increased tension, and on pricking considerable fluid escaped. The brain was not bulging and no evidence of tumor was found. Two attempts at ventricular puncture failed.

During the patient's convalescence from this operation eight abscessed teeth were extracted and his oral hygiene considerably improved. Two months later the choked disks had subsided and the headache was almost completely relieved. He felt so well that he returned home and resumed his professional work. The improve-

ment was only temporary, however, and in May, 1920, the same headaches recurred, usually after mental strain and in the early afternoon, always associated with tense bulging of the decompression area.

In July he returned to Baltimore, once more incapacitated by the severity of the headache. Serologic examination disclosed a negative blood Wassermann; in the cerebrospinal fluid there were eight cells, a weakly positive globulin reaction and a luetic zone gold curve. The spinal fluid Wassermann was negative with 0.2, 0.4 and 0.6 c.c., suggestive positive with 0.8 c.c. and positive with 1.0 c.c. In the absence of Dr. Heuer he was seen by Dr. Walter Dandy, who concurred in our diagnosis of internal hydrocephalus. According to the routine of study used for these cases by Dr. Dandy, intraventricular and intraspinal phthalein and roentgenograms after intraventricular and intraspinal air injections were proposed.

The patient refused all of these procedures except the intraspinal phthalein, which was carried out on July 16. Excretion of dye in the urine was as follows:

First two hours	Trace.	
First fourteen hours	20	per cent.
Second twelve hours	5	"
Third twelve hours	2	"
Fourth twelve hours	1	"
Total (fifty hours)	28	"

Intramuscular phthalein on July 19: 43 per cent. excreted in two hours.

A recent letter informs us that his progress has been much the same. He continues to be partially incapacitated by headaches, which are worse whenever he exerts himself mentally or physically.

Discussion. In a series of papers Dandy and Blackfan[2] [3] and Dandy[4] [5] have thoroughly presented the question of hydrocephalus. Briefly summed up their clinical conclusions are as follows: Internal hydrocephalus can be divided into two anatomically different types, depending on the patency or occlusion of communication between the ventricles and the subarachnoid space. If communication is completely blocked off the hydrocephalus is obstructive. Absorption of cerebrospinal fluid cannot take place from the ventricles though from the subarachnoid space, which the fluid cannot reach, it may be normal. Communicating hydrocephalus results if the obstruction between the ventricular and subarachnoid system is incomplete. Clinically it was shown to occur because of the forma-

[2] Internal Hydrocephalus, An Experimental, Clinical and Pathologic Study, Am. Jour. Dis. Children, December, 1914, viii, 406.

[3] Ibid., December, 1917, xiv, 424.

[4] Extirpation of the Choroid Plexus of the Lateral Ventricles in Communicating Hydrocephalus, Ann. Surg., December, 1918, p. 569.

[5] Experimental Hydrocephalus, Ann. Surg., August, 1919, p. 129.

tion of a barrier of dense adhesions (following meningitis) at the base of the brain, which, while sometimes permitting the passage of fluid from the ventricles to the spinal subarachnoid space, mechanically obstructed its flow to the cerebral subarachnoid space, where most of its absorption should take place. The communicating type of hydrocephalus has been produced in dogs by a perimesencephalic band of gauze, saturated in an irritant which induces adhesions.

The intraventricular introduction of phenolsulphonephthalein will conclusively demonstrate the classification of hydrocephalus. If phthalein is recoverable by spinal puncture within ten minutes thereafter the condition is communicating. Furthermore, absorption and excretion of phthalein injected intraspinally is usually normal, or nearly so, in the obstructive type of hydrocephalus, and is markedly reduced in the communicating type.

Dandy[6] [7] has also introduced the method of roentgenography of the air injected spinal and ventricular systems. This might be expected to show clearly any dilatation of the ventricles, which might be found in either type, as well as the failure of the air to reach the cerebral sulci or the ventricular system if blocked by a band of adhesions at the base as in communicating hydrocephalus.

In this case the diagnosis of internal hydrocephalus is, to our minds, fairly well established because of (1) the character of the headaches; (2) the presence of choked disk; (3) progressive decrease in the pressure and amount of cerebrospinal fluid during the successive punctures of October and November, 1919 (though a fair amount of fluid, somewhat less than normal, could always be recovered); (4) the temporary improvement after decompression; (5) the behavior of the excretion of phthalein injected intraspinally; (6) the striking roentgenoscopic picture.

It is, of course, essential to rule out cerebral or cerebellar neoplasm or cyst. The existence of such a lesion seems improbable because of the history of sudden onset, the lack of progress in the disease and the absence of localizing signs. It is probable that here the obstruction is only partial and that a certain amount of ventricular fluid is allowed to flow into the spinal system. It is unfortunate that roentgenoscopic studies of the air filled ventricles and spinal canal were not permitted. Such studies would have made the diagnosis more definite.

Unfortunately, also, the ventricular injection of phthalein was not permitted. This would have allowed a demonstration of the patency of the foramina between the ventricular and the subarachnoid systems. The intraspinal injection of phthalein did, however, afford the information that only a small part of the subarachnoid space was participating in the absorption of cerebrospinal

[6] Ventriculography following the Injection of Air into the Cerebral Ventricles, Ann. Surg., July, 1918, p. 5.

[7] Roentgenography of the Brain after the Injection of Air into the Spinal Canal, Ann. Surg., October, 1919, p. 397.

fluid. Normally, after intraspinal phthalein 35 to 60 per cent. is excreted in two hours. In this patient there was but a trace in two hours and only 28 per cent. was excreted in forty-eight hours.

Having concluded that in all probability the patient's headaches are due to internal hydrocephalus of the communicating type, questions arise as to the etiologic factors which produced this condition. Syphilis has, of course, been suggested by various authors, and is particularly noteworthy as a cause of infantile hydrocephalus. A syphilitic process which will almost completely occlude the foramina of exit of the cerebrospinal fluid from the ventricular system, or which will so affect the meninges as to produce a dense band of adhesions around the base of the brain, must in the adult be relatively uncommon, as few such cases of hydrocephalus in adults are observed. The possibility of such a condition due to syphilis is, however, admittedly academic. On the other hand the time relation of the first intraspinal injection to the onset of the characteristic headache stands out very strikingly. It must be admitted that for some time we failed to be impressed by this possible relation of cause and effect; but later consideration has urged upon us the conclusion that the first intraspinal injection given the patient set up a severe meningitis, which, since he survived it, was probably aseptic. This in healing produced a mass of adhesions about the subarachnoid space, causing a partial occlusion of one or more of the three foramina of exit from the fourth ventricle. Such a phenomenon must, however, be extremely rare, since we have been unable to find similar cases in the literature and since our own fairly large experience affords no like example.

The hydrocephalus in this case is of the communicating type, since there are periods of freedom from both headache and the bulging of the decompression area and since a fair amount of spinal fluid was usually obtainable at the time of puncture. The phthalein absorption is characteristic in that it was markedly reduced.

So far as treatment is concerned there would seem to be little to be done. The operation of choroid plexectomy is hazardous; according to Dandy it is impossible to break up adhesions at the base because of their inaccessibility. One can hope for a spontaneous cure. To quote Dandy and Blackfan:[8] "It is not difficult to imagine recovery following the gradual disappearance of adhesions. It is also possible to imagine a sudden rupture of the thin wall of a large fourth ventricle cyst, producing a new foramen of exit to the subarachnoid space."

Summary. 1. There is presented a case of communicating internal hydrocephalus in a neurosyphilitic.

2. The hydrocephalus appears to stand in the relation of effect and cause to an intraspinal treatment with mercurialized serum.

3. A possible though remote danger of intraspinal therapy is pointed out.

[8] Loc. cit.

OZENA AND ITS RELATION TO TUBERCULOSIS.

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Although not an uncommon disease, ozena has been relegated so strictly to the sphere of the rhinologist and the laryngologist that it is but little known outside these specialties. For a great many years there have been scattered references in the literature pointing out the frequency with which ozena and tuberculosis are to be observed in the same patient. This fact has been recognized in a general way, but has by no means been accorded the attention it deserves. Recent work done along these lines emphasizes the necessity of a more general knowledge of the symptomatology and therapy of ozena on the part of the medical profession as a whole. The frequent incidence of tuberculosis in ozenatous patients makes it of as much importance for the internist to recognize and examine a case of ozena as a possible subject of pulmonary involvement as it is for the nose and throat specialist to be familar with the various systemic diseases, of which derangements in his own particular field of observation are only part and parcel.

It will be the object of the following paragraphs to set forth the evidence at hand concerning the coincidence of these two diseases, together with the results of some experimental work done on the subject in the department of laryngology of the Johns Hopkins Hospital.

The word "ozena" is derived from the Greek, and means literally a stench. The lesions are confined to the mucous membranes of the nose, pharynx and may extend to the larynx. It is characterized by the formation of greenish-black crusts, with a sickening odor. It usually begins in childhood and runs a progressive course, tending to become less severe as old age advances. A predilection for filth makes it more common among the lower classes. Children of ozenatous parents are often found to be suffering with the same malady, and there is considerable evidence to show that it is contagious. The appearance of a well-developed case is often one of marked cachexia and malnutrition.

In the first stages there is a transient hypertrophy of the turbinates. Eventually the mucous membrane lining of the whole nose undergoes atrophy and all lymphoid and secretory structure disappear completely. Ulceration is not the rule. An idea of the profound changes that take place in the histological picture may be gained from the accompanying photomicrographs. Fig. 1 shows a section through the mucous membrane of a comparatively normal

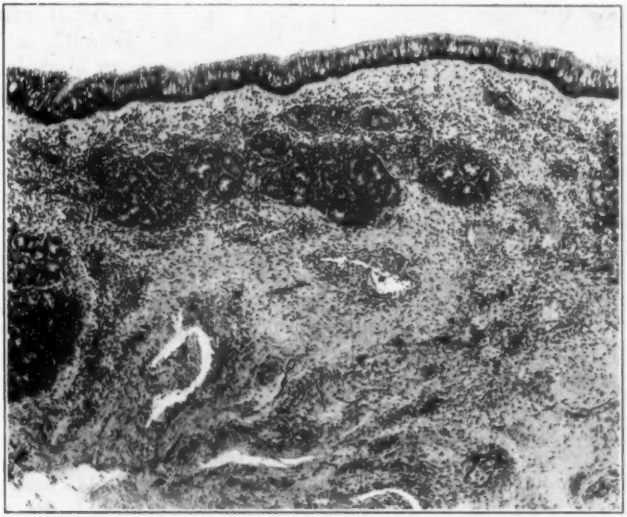

FIG. 1.—Section through the mucous membrane of a comparatively normal middle turbinate, showing columnar epithelium and glandular structures.

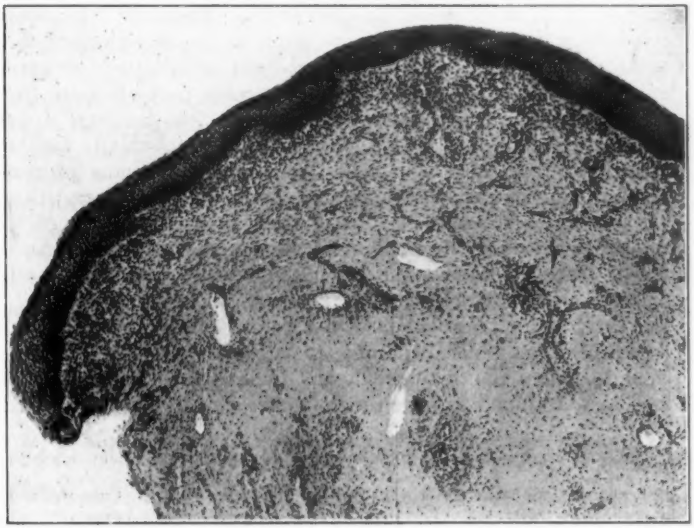

FIG. 2.—Section through the mucous membrane of the middle turbinate taken from a case of ozena, showing the stratified epithelium and entire absence of glandular structure. There is no evidence of tubercle.

middle turbinate. Note the stratiform ciliated cylindrical columnar epithelium with goblet cells interspersed. Beneath is the basement membrane and finally the tunica propria of fibro-elastic tissue with its venous plexuses and tubo-alveolar glands. Contrast this with Fig. 2. One can scarcely realize they are from the same anatomical locality. The stratiform columnar epithelium has been entirely replaced by a layer of stratified epithelium desquamating on the surface. Polymorphonuclears and small round cells are fairly abundant in this layer and in the one immediately below it, which corresponds to the submucosa. In the deeper structures, plasma cells, fibroblasts and eosinophils are found. There are numerous bloodvessels and venous plexuses. The striking feature is the complete absence of all glandular and secretory structure so abundant in the normal nose. Note will also be made of the complete absence of any structure resembling tubercle.

Many organisms have been mentioned in connection with the etiology of ozena. Among the better known are (1) the Abel-Löwenberg[1] bacillus, described by Abel in 1893, and (2) the cocco-bacillus fetidus ozenæ discovered by Perez,[2] and with which he claimed to have reproduced in rabbits lesions characteristic of ozena. The third organism identified with the disease is an acid-fast bacillus, and it is concerning the significance of this organism in the nasal secretions of ozena that a great deal of the controversy of recent years has had to do. Although it has long been known that such bacteria are found in the secretions of the ozenatous nose, they have in general been looked upon as accidental, just as similar flora with acid-staining properties are frequently present in sebaceous secretions, in the discharge from chronic ears, etc. Not everyone, however, admits this to be the case. There are those who hold that the acid-retaining properties of this particular bacillus have a more sinister meaning; that if it is not the tubercle bacillus it bears such a resemblance to that organism as to demand more than a casual notice. And, indeed, there is considerable ground for their contention, both clinically and bacteriologically.

As early as 1882 Fränkel[3] collected from the literature records of 6 cases of ozena which had come to section. Five of these were found to have definite tuberculosis. In Alexander's[4] series of 22 cases 15 were found to have died of tuberculosis. On the clinical

[1] Bakteriologische Studien über Ozaena Simplex, Centralblatt für Bakteriologie, 1893, xiii, p. 161.

[2] Recherches sur la bacteriologie de l'ozena, Annals de l'Institut Pasteur, 1899, xiii, p. 937.

[3] Pathologische Mittheilungen, ii Beiträge zur Rhinopathologie, Virchows Arch., 1882, lxxxvii, p. 285.

[4] Die Bezeihungen der Ozaena zur Lungentuberculose nebst Bemerkungen über die Diagnose der Ozaena, Arch. f. Laryngol. u. Rhinol., 1903, xiv, p. 1.

side there is even more significant evidence. Alexander in the paper quoted above found a family history of tuberculosis in 16 of 22 cases. Wingrave[5] found a similar history in 37 out of 60 cases. Caboche[6] found a family history of phthisis in 16 of his 39 cases. In our own series 4 of the 8 cases in which a family history was obtained were found to have tuberculous antecedents.

The incidence of tuberculosis in people suffering with ozena is just as striking. Alexander in the same monograph records 50 cases of ozena in which definite pulmonary tuberculosis was found in 22, suspicious tuberculosis in 7 and pulmonary lesions of a different character in 4. Theisen[7] found phthisis in 7 out of 20 cases of ozena. McKenzie[8] in 34 cases found 5 with pulmonary tuberculosis and 3 with other tuberculous manifestations. Mackeith[9] found "phthisis pulmonalis" in 4 out of 13 cases. In our own series of 9 cases 3 showed frank pulmonary tuberculosis and 3 evidence of less active lesions. In other words, 40.4 per cent. of the cases cited above showed a more or less definite clinical tuberculosis and 56.6 per cent. gave a family history of phthisis.

These figures would certainly indicate something more than a mere accidental association of the two diseases. What then is this relationship? Before attempting an answer let us return to a consideration of the acid-fast organisms found in the crusts in ozena.

The tinctorial qualities of these bacilli can be demonstrated in almost all true cases of ozena. We have not found them in other diseases simulating ozena, such as syphilis of the nose. When found they are most abundant in the thick black crusts of a fully developed case. The best preparations are obtained by taking a bit of the crust, dissolving it in sterile salt solution and spreading it on a slide with a platinum loop. Fix by passing several times through a flame. Overheating will cause the organisms to swell and become distorted. Stain in the usual manner by the Ziehl-Neelsen method.

Owing to the fact that many of these bacilli are not alcohol-fast, it is best to decolorize only in an acid bath, using 25 per cent. sulphuric acid. The preparation is counterstained with methylene blue. The acid-fasts will be found to stand forth a bright red in contrast to the blue of the other organisms. They vary greatly in their morphology, ranging all the way from streptothrix-like clumps

[5] Atrophic Rhinitis, Journal of Laryngology, Rhinology and Otology, 1894.

[6] L'ozéne forme larvée de la tuberculose, Ann. d. mal. d. l'orielle, du larynx (etc.), 1917, xxxiii, pt. ii, p. 260.

[7] Etiology and Diagnosis of Ozena and its Relation to Pulmonary Tuberculosis, Albany Medical Annals, 1904, xxv, p. 140.

[8] Atrophic Rhinitis (Ozaena) and Tuberculosis, Journal of Laryngology, Rhinology and Otology, 1916, xxxi, p. 176.

[9] Atrophic Rhinitis (Ozaena) and Tuberculosis, Pt. ii, Tuberculin in Atrophic Rhinitis, Journal of Laryngology, Rhinology and Otology, 1916, xxxi, p. 232.

to short, thick rods. They frequently occur as thin, curved, beaded rods, identical in appearance with the tubercle bacillus.

With the assistance of Dr. Esau Greenspon, of the pathological department, an attempt was made early in the year 1918 to cultivate these organisms. Crusts were washed several times in sterile saline solution and implanted on Dorset egg medium, sheep serum agar, blood agar and other media. Unfortunately for our work Dr. Greenspon was called to the colors at this time, and this fact, coupled with other exigencies brought on by the war, forced us to abandon this phase of the work. However, the organisms in question have been isolated and grown by Wingrave,[10] using Dorset egg medium reinforced with ozena crusts.

Animal Experiments. In the paper last quoted there is, furthermore, recorded an account of guinea-pig inoculations. Six animals were injected, using a reinforced emulsion made from ozena crusts. At section the 3 animals which had been injected intraperitoneally were found to have escaped all infection. The 3 which had been inoculated subcutaneously showed definite tuberculosis, with caseation of glands, giant-cell formation and "tubercle bacilli in and around the giant cells."

Our experiments along these lines have not been so successful. Crusts were collected from 5 cases of ozena in which we had first demonstrated the presence of acid-fast bacilli. An emulsion of the crusts was made from each case and 3 c.c. of this injected into guinea-pigs, using 2 animals to each patient. The intraperitoneal method was used. At the end of four weeks several animals had died of intercurrent infections—no gross signs of tubercle were found at autopsy. Smears and sections from various organs were stained with similar results. The remaining animals were sacrificed at the end of six weeks. No signs of tuberculosis were found. A second group was inoculated, with the same disappointing results. Recently a third series of animals was injected, using material from one new and two old cases. This time the emulsion was introduced subcutaneously. The regional lymph glands became swollen within a week. The animals died during the fourth and fifth weeks. They were carefully examined, but no histological evidence of tubercle was found in the glands or viscera.

As before mentioned we first ascertained the presence of the acid-fast organisms in the material used. Arguing from the well-known susceptibility of the guinea-pig to the tubercle bacillus we are forced to conclude, from our experiments, that the acid-fast bacillus found in the nasal secretions of ozena is not identical with the tubercle bacillus.

Tuberculin Therapy.—It would entail too much space to go into the many methods advocated in the treatment of ozena. Their

[10] Atrophic Rhinitis (Ozaena) and Tuberculosis, Pt. iii, The pathological Aspect, Journal of Laryngology, Rhinology and Otology, 1916, xxxi, p. 276.

very number and diversity are an indication of our lack of true information on the subject. In general there are two classes of therapy employed. Local measures in the form of irrigations, suppositories, instillations and paraffin injections. In the second group fall the various forms of vaccinotherapy. The first class of remedial agents acts apparently in a purely mechanical manner and are efficacious only so long as one persists in their use.

Results of a more lasting character are claimed from the use of vaccines. Hofer and Kofler,[11] using a vaccine made from the Perez bacillus, reported favorable results. Subsequent reports on the use of this vaccine conflict. Golgau[12] experimented with seven different varieties of vaccines, and from his results concludes that all such forms of therapy are of little or no value. Mackeith,[13] starting with the premise that ozena is a tuberculous manifestation, has treated a series of 13 cases with tuberculin. His results have been very good. Some of these patients have been under observation as long as two and a half years after treatment was inaugurated. Of these 7 showed great improvement, 3 improvement, 2 suffered relapse and 1 case was not benefited.

In January, 1918, we mailed cards to about 100 names indexed in the nose and throat dispensary under the headings "Ozena" and "Atrophic Rhinitis." Of this number about 40 reported for examination. Our task was to pick out only those which we considered to be genuine cases of ozena. We chose as our more important criteria the characteristic fetor, atrophy of the mucous membranes and the presence of the greenish-black crusts in the nose. When possible smears were made to determine the presence of acid-fast bacilli. From this group we have been able to obtain fairly complete records of 9 cases of what we consider to be true ozena. As the patients reported they were given the routine nose and throat examination, including roentgen ray of the sinuses and Wassermann test. Of the 9 cases, 7 consented to undertake the tuberculin treatment, for the administration of which as well as for the chest examinations we are indebted to the Phipps Tuberculosis Dispensary.

The tuberculin used was the human bouillon filtrate. An initial dose of from $\frac{1}{100000}$ to $\frac{3}{100000}$ mg. was given and the dosage increased gradually until at the end of a year the patient received 1000 mg. each month. A glance at the following abstracts will give an idea of the success that has attended our treatment of ozena with tuberculin:[14]

[11] Bisherige Ergebnisse einer neuen Vakzinationstherapie bei Ozena (Cocco bacillus fetidus ozena Perez), 1913, xxvi, No. 42, p. 1698.

[12] Vaccine Treatment of Ozena, Laryngoscope, 1918, xxviii, p. 380.

[13] Loc. cit.

[14] These observations were carried up to September, 1920.

CASE I.—H. K., male, white. Birthplace, United States. Laborer. Aged twenty-nine years. Complaint: "Pimple in the nose." Admitted January 3, 1918.

Family History. Negative.

Past History. Negative, except for chronic nasal discharge.

Personal Examination. Temperature, 99.2°. *Roentgen-ray sinuses,* negative. *Wassermann,* negative. *Glands,* not enlarged. *Nose,* inferior turbinates atrophied; both sides filled with foul-smelling discharge and greenish crusts. *Smear* from nose showed numerous acid-fast bacilli. *Chest Examination:* slight impairment to the third rib on the right and left and throughout the back. Breath sounds diminished. *Von Pirquet test* slightly positive. *Roentgen ray of chest:* spotty infiltration of both lungs, especially on the right side, tuberculous in origin. *Diagnosis:* possibly some fibrosis of both uppers.

Course. At the end of three months, during which time he was seen weekly, this patient showed a marked improvement. The discharge disappeared almost entirely and lost its disagreeable odor. His general health became better, with improvement in appetite and a gain of ten pounds in weight. From this time to the present his condition has remained about stationary. He now receives the maximum dose of 1000 mg. each month. He has discontinued all irrigations and other treatment.

CASE II.—A. L., male, white. Birthplace, United States. Schoolboy. Aged thirteen years. Patient referred for consultation from the Phipps Tuberculosis Dispensary December 27, 1917.

Family History. Mother has tuberculosis. One sister died of tuberculosis.

Personal History. Scarlet fever and diphtheria in infancy. Profuse discharge in nose for some time.

Personal Examination. Temperature, 99.2°. *Wassermann,* negative. *Glands,* not enlarged. *Nose,* middle turbinates atrophied; dry, foul-smelling discharge throughout the nose. *Tonsils,* not enlarged. *Chest Examination:* manubrial dulness; impairment to second rib and to the lower angle of the scapula behind. *Impression,* mediastinitis. *Von Pirquet,* positive. *Roentgen ray chest,* marked fibroid infiltration of the right lung; probable thickening of the pleura. *Diagnosis:* changes probably tuberculous in origin.

Course. Patient has been under tuberculin treatment for a year. The odor has disappeared and the discharge has practically ceased. He has gained in weight. At present is receiving 1000 mg. of tuberculin each month.

CASE III.—M. F., female, negress. Birthplace, United States. Aged eighteen years. *Complaint,* nasal discharge.

Family History. None obtainable.

Personal History. Nasal trouble for past year.

Personal Examination. Wassermann, negative. *Roentgen-ray sinuses*, clouding both antra. *Glands*, not enlarged. *Nose*, inferior turbinates atrophied; thick, greenish crusts with typical fetor. *Tonsils*, atrophic. *Nasopharynx*, walls covered with greenish crusts. *Smear* from the nose showed acid-fast bacilli in large numbers. *Chest Examination:* possible minimal left apical tuberculosis; rales heard.

Course. After an irregular course of treatment for three months the patient returned and volunteered the information that her subjective symptoms had disappeared. Examination of the nose showed practically no discharge and no odor. The patient could not be prevailed upon to continue treatment.

CASE IV.—M. V., female, white. Birthplace, United States. Schoolgirl. Aged fourteen years. *Complaint*, sunken nose. Admitted June 25, 1919.

Family History. One sister has nose trouble (ozena).

Personal History. Nose has been "sinking for several years;" offensive discharge; complete anosmia.

Personal Examination. Temperature, 98.8°. *Wassermann*, negative. *Roentgen-ray sinuses*, infection of right frontal, ethmoids and antrum. *Glands*, just palpable in anterior and posterior triangles. *Nose*, external deformity; interior filled with thick, black crusts with a disagreeable odor; atrophy of both inferior turbinates; antra irrigated and fluid returned clear. *Smear* from nose showed numerous acid-fast bacilli. *Chest examination*, negative. *Von Pirquet*, slightly positive.

Course. There was an apparent flare-up of the nasal condition and some local reaction after the first seven injections of tuberculin. At the end of six months the discharge had practically disappeared together with the odor.

About one year from the time the treatment was commenced the patient suffered a relapse, with a return of the discharge and odor. She is still under treatment.

CASE V.—C. G., female. Birthplace, United States. Occupation, housework. Aged twenty-three years. *Complaint*, trouble with nose and throat. Admitted March 5, 1918.

Family History. Negative.

Personal History. Occasional headache. Post-nasal discharge for two years.

Personal Examination. Temperature, 97.8°. *Wassermann*, negative. *Roentgen-ray sinuses*, negative. *Glands* are just palpable in the posterior triangles of the neck and at the angles of the jaw.

Nose, atrophy of both inferior turbinates; profuse purulent discharge on both sides, with odor. *Tonsils*, atrophic. *Chest Examination*, negative for tuberculosis.

Course. After five months' treatment with tuberculin the patient reports that she thinks the discharge is considerably less. Examination shows a slight amount of discharge on the left side. *It is worthy of note that nine months after first being seen this patient developed pulmonary tuberculosis while under observation.*

CASE VI.—M. C., female. Birthplace, United States. Schoolgirl. Aged ten years. *Complaint*, nasal odor and nasal discharge. Admitted October 25, 1919.

Family History. Mother has pulmonary tuberculosis.

Personal Examination. Wassermann, negative. *Roentgen-ray sinuses*, negative. *Glands*, not enlarged. *Nose*, foul, greenish crusts in the posterior nares and in the nasopharynx. All turbinates atrophied. *Smear* showed numerous acid-fasts. *Chest examination*, negative. *Von Pirquet*, negative.

Course. After five months' treatment with tuberculin, the nose shows only a small amount of discharge on the right side. Odor not marked. From this time until the present date the patient has suffered several remissions. At no time, however, has her condition been as bad as when first seen.

CASE VII.—J. R., male. Birthplace, United States. Clerk. Aged twenty-eight years. *Complaint*, atrophic rhinitis.

Family History. Mother died of pulmonary tuberculosis.

Personal History. Had attacks of chills and fever for eight years. Cough and pain in chest. Formation of foul-smelling crusts in the nose since childhood. Anosmia.

Personal Examination. Glands are just palpable at the angles of the jaws. *Nose*, septum deflected to the right; left side filled with typical foul-smelling discharge. *Pharynx*, purulent discharge on the posterior wall. *Sinuses* are clear. *Smear* from nose showed acid-fast bacilli in large numbers. *Chest examination*, breath sounds and percussion note impaired at both apices. (Examination made outside the hospital.)

Course. After three months' treatment with tuberculin the patient reported for examination. He says that those with whom he is in daily contact no longer complain of the odor. Examination of the nose showed about half the amount of discharge first noted.

CASE VIII.—F. K., white. Birthplace, Bohemia. Occupation, farmer. Aged forty-seven years. *Complaint*, throat trouble. Admitted November 6, 1918.

Family History. Negative.

Personal History. Cough for one year.

Personal Examination. Glands not palpable. *Nose*, turbinates atrophied; discharge, with fetid odor.

Chest Examination. Impairment of the upper right and left; rales on the left side. *Tubercle bacilli* present in the sputum. *Roentgen ray chest*, spotty infiltration of left upper and right apex. *Diagnosis*, pulmonary tuberculosis. In this patient the onset of tuberculosis and ozena were apparently simultaneous.

Course. Not treated for nasal condition.

CASE IX.—E. S., male, white. Birthplace, United States. Aged sixty-nine years. *Complaint*, catarrh and deafness. Admitted May 10, 1920.

Family History. Probable history of tuberculosis and ozena in family.

Personal History. Nasal discharge since early adult life.

Personal Examination. Temperature, 98.4°. *Wassermann*, negative. *Roentgen-ray sinuses*, clouding of left frontal and ethmoids. *Glands*, not enlarged. *Nose*, inferior turbinates atrophied; middle turbinates, covered with thick, greenish crusts, with foul odor. *Nasopharynx* shows same picture as nose.

Chest Examination. Fibroid changes over uppers; marked on right side; few persistent rales above right clavicle. *Roentgen ray*, old fibroid tuberculosis of left upper.

Course. Not treated.

To summarize:

Cases I and II show great improvement two and a half years after treatment was started.

Cases III and VII show improvement after three months' treatment.

Case V showed an initial improvement after five months' treatment. Four months after stopping treatment she developed pulmonary tuberculosis.

Cases IV and VI showed an initial improvement followed by relapse—No. IV after one year's treatment and No. VI after five months' treatment.

By improvement we mean cessation of discharge and a better condition of health in general. In none of the cases was the atrophy in the nose affected. In some the sense of smell returned to a certain extent.

The good results reported from the use of other vaccines make us wary of attributing to the tuberculin any specific action on the nasal condition. At any rate whether the amelioration of symptoms following the use of tuberculin be due to a general tonic action or is the result of the introduction of a foreign protein into the blood or whether there is some direct action on the nasal disease is beside the question. The fact remains that of the various remedies we have heretofore tried in the treatment of ozena by far the best results have been obtained with the use of tuberculin.

Our results and those of Mackeith certainly warrant a more extensive trial of this form of therapy.

As intimated before, our main object has been to point out and insist upon the relation that exists between the disease ozena and tuberculosis.

We offer as evidence from our own and cases collected from the literature:

28 cases that have come to autopsy, tuberculosis was found in 20 and was the cause of death in 15 of these.

129 cases in which a family history of tuberculosis was demonstrated in 73.

126 cases in which definite clinical tuberculosis was found in 52.

It is true our laboratory tests argue against any etiological identity. On the other hand the clinical evidence cannot be dismissed as falling within the realm of coincidence. The question of the etiology of ozena has yet to be settled. That the disease is very frequently associated with tuberculosis is a fact—a fact that it behooves every practising physician to bear in mind and one that should cause him to investigate every case of ozena coming under his notice as a possible instance of tuberculosis.

DIABETES MELLITUS, SYPHILIS AND THE NEGRO.

By I. I. Lemann, M.D.,
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In view of Warthin's report that he has found syphilitic pancreatitis in all of the diabetic cases at the University of Michigan coming to autopsy, it has seemed worth while to examine from this point of view a material rich in syphilis. Warthin's[1] statement is "that diabetes may be associated with the more marked degrees of syphilitic pancreatitis, and in our autopsy series all of our diabetic cases have been so associated, but that a number of syphilitic pancreatitis of similar degree of severity have not presented the clinical symptoms of diabetes. It seems very probable, therefore, that latent syphilis is the chief factor in the forms of pancreatitis most frequently associated with diabetes, but that diabetes is not always associated with severe degrees of this type of pancreatitis." Since this report was made there has been very little discussion of the matter in the literature, though Warthin's contention has not gone altogether unchallenged. Thus, J. R. Williams[2] reported that only 4 out of 143 cases of diabetes mellitus gave a positive Wassermann and the

[1] Am. Jour. Med. Sc., 1916, cli, 157.
[2] Jour. Am. Med. Assn., 1918, lxx, 365.

physical examination of 126 out of the total 143 patients did not lend support to the view that syphilis is a common causal factor in diabetes. Jacob Rosenbloom[3] reported that in 62 cases of diabetes he found positive evidence (including positive Wassermanns) in 7, or only 10.3 per cent. Five of the 7 patients were persuaded to take syphilitic treatment. There was no increase in the carbohydrate tolerance in any of these cases after treatment. Anna I. Van Saun[4] investigated the blood from 72 known diabetics. Only 1 gave a positive Wassermann reaction; 52 gave a negative reaction, 2 a doubtful reaction and in 19 cases the controls failed to hemolyze, so that no readings could be made. The one serum giving a positive reaction was that of a patient giving a history of syphilis. Of the 2 doubtful reactions 1 was a patient with a history of chancre twenty-six years previously; the other patient gave no history of syphilis.

My own experience in private practice has given me the same impression that syphilis is seldom the cause of diabetes mellitus. In such cases where lues does certainly exist we must consider whether it is present simply as a concomitant affection or as the real cause of the diabetes. Only once in my series did antisyphilitic treatment have any effect upon the carbohydrate tolerance, which is in agreement with the experience of Rosenbloom already quoted. It is perfectly apparent that a diabetic may have or may acquire syphilis just as he may acquire tuberculosis or typhoid fever, but that is quite different from the situation of the syphilitic who because of his syphilitic pancreatitis presents the phenomena of diabetes mellitus. It is not denied that syphilitic pancreatitis may present the clinical picture of diabetes mellitus; but my present thesis is that such cases represent the exception and not the great body of diabetic patients. It is in support of this contention that the results of this statistical study are presented.

The syphilization of the negro is a matter of common knowledge to all practitioners in the South. They present a material enormously rich in every aspect of the disease, because, owing to their ignorance and poverty, they go frequently untreated or inadequately treated. They are more liable even than other patients to disappear from view when their immediate pressing symptoms have been relieved to reappear when the disease has later made vast inroads. If therefore syphilitic pancreatitis is the common cause of diabetes mellitus we should find the latter disease more prevalent among them than among the whites. This, however, is not the case. Indeed, it was formerly thought that diabetes mellitus was relatively rare in the negro. While this disease is not rare in the negro, still the incidence is not as great among them as among the whites. This I showed ten years ago from a study of the reports of the

[3] Jour. Am. Med. Assn., 1917, lxviii, 1232.
[4] Jour. Med. Research, 1917, xxxvii, 205.

Charity Hospital at New Orleans covering twelve years (1898–1909). There were 45 white diabetics and 19 negro diabetics in 61,298 admissions. The negroes furnished 40 per cent. of the admissions and only 30 per cent. of the diabetics. The total incidence was 0.63 per thousand. The incidence among the whites was 0.72 per thousand while among the negroes it was only 0.47 per thousand.

TABLE I.—DIABETES MELLITUS IN CHARITY HOSPITAL, 1898–1909.

Year.	White cases.	Negro cases.	White admissions.	Negro admissions.	Total. admitted.
1898	2	5	4,738	2,996	7,734
1899	5	0	5,068	3,412	8,480
1900	4	0	4,614	3,114	7,728
1901	7	3	4,657	3,068	7,725
1902	7	2	4,928	3,248	8,176
1903	6	3	4,767	3,434	8,201
1904	2	0	5,300	3,299	8,689
1905	2	1	5,091	3,221	8,412
1906	1	0	5,027	3,425	8,452
1907	4	3	5,294	3,556	8,950
1908	3	2	5,874	3,666	9,540
1909	2	2	5,850	3,726	9,576
	45	19	61,298	40,265	101,565

0.72 per 1000. 0.47 per 1000. White and negro, 0.63 per 1000.
Percentage of diabetics: White, 70 per cent.; negro, 30 per cent.
Percentage of admissions: White, 60 per cent.; negro, 40 per cent.

A review of the figures for the years 1910–1919 confirms the impression obtained for the earlier period in a remarkably accurate way. In 160,044 admissions there were 135 white diabetics and 59 negro diabetics. The negroes furnished 43 per cent. of the admissions and only 30 per cent. of the diabetics, practically the same relation as in the former period.

TABLE II.—DIABETES MELLITUS IN CHARITY HOSPITAL, 1910–1919.

Year.	White cases.	Negro cases.	White admissions.	Negro. admissions.	Total admitted.
1910	11	0	6,719	4,594	11,313
1911	20	7	7,314	4,906	12,220
1912	15	5	7,838	5,145	12,983
1913	5	3	8,405	5,944	14,349
1914	19	9	9,700	7,042	16,742
1915	8	7	9,897	7,926	17,823
1916	21	11	10,111	8,540	18,651
1917	13	9	10,908	8,686	19,651
1918	15	4	11,359	7,862	19,221
1919	8	4	9,789	7,359	17,148
	135	59	92,040	68,004	160,044

1.4 per 1000. 0.86 per 1000. White and negro, 1.2 per 1000.
Percentage of diabetics: White, 70 per cent.; negro, 30 per cent.
Percentage of admissions: White, 57 per cent.; negro, 43 per cent.

TABLE III.—INCREASE IN DIABETES MELLITUS AT CHARITY HOSPITAL.

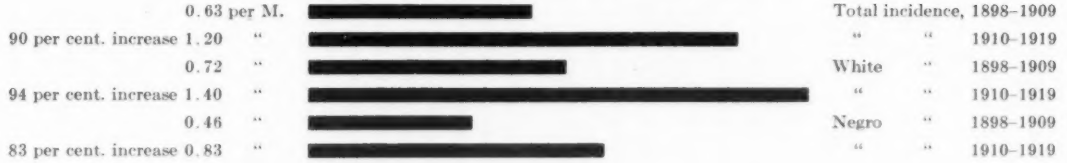
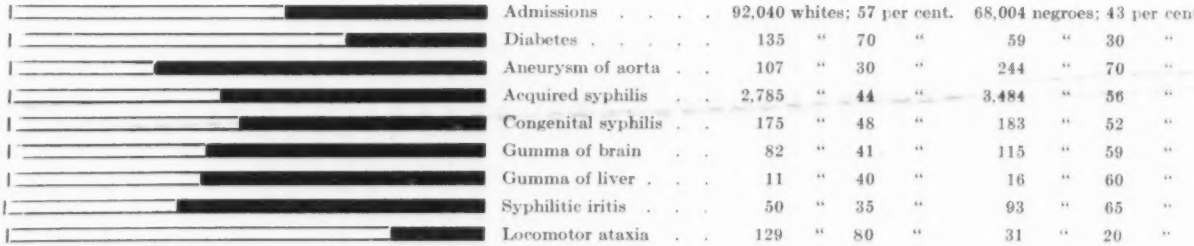


TABLE IV.—CHARITY HOSPITAL, 1910–1919.


Admissions . . . . 92,040 whites; 57 per cent. 68,004 negroes; 43 per cent.
Diabetes . . . . . 135 " 70 " 59 " 30 "
Aneurysm of aorta . . 107 " 30 " 244 " 70 "
Acquired syphilis . . 2,785 " 44 " 3,484 " 56 "
Congenital syphilis . . 175 " 48 " 183 " 52 "
Gumma of brain . . 82 " 41 " 115 " 59 "
Gumma of liver . . . 11 " 40 " 16 " 60 "
Syphilitic iritis . . . 50 " 35 " 93 " 65 "
Locomotor ataxia . . 129 " 80 " 31 " 20 "

A striking fact is well illustrated in Table III. The incidence of diabetes mellitus has risen here as it has elsewhere, as has been reported by Joslin and others. The burden of the increase has been borne fairly equally by the whites and the negroes, and whatever cause is operating to produce this increase has affected both races alike. The total incidence has risen from 0.63 per thousand to 1.2 per thousand (90 per cent.); the white incidence from 0.72 per thousand to 1.4 per thousand (94 per cent.) and the negro incidence from 0.47 to 0.86 per thousand (83 per cent.). It can hardly be fairly contended that syphilis has been a more potent factor in the production of diabetes in the last decennium than in the preceding one. Moreover if it were, the heavier burden should have fallen upon the more intensely syphilized race. Since it fell upon both races approximately alike, it would be most plausible to seek the explanation in some factor affecting both alike and operating in increasing intensity. Syphilis hardly complies with these conditions.

That it does not comply with these conditions may be made evident from a study of the ravages produced by syphilis in other parts of the body in the white and negro respectively. Although the negroes form about 40 per cent. of the admissions to our hospital and furnish only 30 per cent. of the diabetics, they furnish more than 50 per cent. of all the syphilitic diseases. This I have tried to show graphically in Table IV.

The only exception to the rule that the negro furnishes more than his relative share of any syphilitic disease is locomotor ataxia. Dr. R. M. Van Wart (personal communication) informs me that this is in accordance with his clinical experience and that of other neurologists of the South. While the negro by no means shows even a relative immunity to luetic infection of the central nervous system, still he does show a relative decreased incidence of locomotor ataxia. It would appear, therefore, that we must accept one of two explanations of the smaller incidence of diabetes among the negroes and its possible relation to the theory of syphilitic pancreatitis as a common cause of diabetes mellitus:

1. There is no relation between the incidence of diabetes mellitus and syphilis; hence there is no probable etiologic relation between the two.

2. There is an unexplained immunity of the negro race to the production of spirochetal pancreatitis just as there is an unexplained immunity of the race to the production of locomotor ataxia.

I am convinced of the validity of the former alternative for the reasons set forth in this communication. The assumption of the second alternative would leave unexplained the increased incidence of diabetes mellitus in both whites and negroes and the fact that this incidence has increased equally in both races.

STUDIES ON THE DOSAGE OF DIGITALIS IN CHILDREN.

By Hugh McCulloch, M.D.,
and
Wayne A. Rupe, M.D.

(From the Department of Pediatrics, Washington University, School of Medicine.)

Purpose. We have attempted to determine the amount of tincture of digitalis that is necessary to produce certain effects on the heart of children in order to establish whether the relation between body weight and dosage that has been recently established for adults is directly applicable to children, or if not, what modifications are necessary in order to base the dosage of the tincture of digitalis on the body weight of children of various ages and weights. As a result of our observations in thirty-six children, we have noticed certain effects that are worthy of mention and emphasis.

Introduction. Since the introduction of accurate methods of standardization of digitalis, it has been found that by the careful administration of large doses of the drug, effects on the human heart can be obtained within a very short time. Very typical and definite physiologic effects may be observed after two to five hours. It has been found necessary and advisable to use standard amounts of the drug, otherwise unsatisfactory and even unfortunate results might result when large doses are given. Eggleston[1] has advocated the use of formulæ from which the dose of standardized preparations of dried leaves, tincture or infusion may be estimated. The dose of the tincture is estimated according to body weight, 0.15 of a cat unit being given for each pound. The effects of the drug can be determined through its toxic action, which produces vomiting and alterations in the electrocardiogram. These alterations are notable delay in conduction from auricles to ventricles, alteration in the form of the *T* wave and the appearance of premature ectopic beats. The estimation of the dose is based on findings made in the pharmacologic laboratory on cats after intravenous administration of the drug. To apply the method to human beings and to change the method of administration of the drug from intravenous injections to oral administration may involve some alteration in the amount necessary to produce an effect. The dosage should be the amount of drug sufficient to produce an optimum therapeutic effect and just below the amount that would produce toxic effects. In the methods mentioned no account is taken of the possibility of any variation in the response to digitalis, with variations in age or body weight, over such wide limits as in children and adults. It has not been shown that hearts show appreciable variation in the

[1] Arch. Int. Med., 1915, xvi, 1.; Jour. Am. Med. Assn., 1920, lxxiv, 733.

character of their response to digitalis even though the hearts be from species widely separated; for example, frogs, cats or human beings. It is quite possible that the method of administration may lead to some variation. The theoretic dosage for children has been the same for adults, due allowance being made for difference in body weight.

Method. The drug employed has been the tincture of digitalis obtained in the open commercial market and kept for general use. It has been standardized according to the cat method of Hatcher and Brodie,[2] has been kept under conditions that prevent an appreciable depreciation in its potency and has been standardized at intervals. Only small amounts sufficient to last a few days were dispensed to the wards for use. The cat standardization of the tincture has shown that one cat unit averaged 1 c.c.

The patients selected were in the St. Louis Children's Hospital for various complaints, none of which were of such a nature at the time of the administration of digitalis to confine the patient to bed. None of the patients were suffering from recognizable heart disease nor from any condition that might have any effect on the heart. As far as could be determined the hearts were normal.

For the purpose of observation the patients were confined to bed or allowed very limited periods in a wheel chair or sitting about the wards. The children were all somewhat below normal weight for their age, though not to such an extent as to influence the action of the drug; nor was there any abnormality or disturbance in the gastro-intestinal tract. Electrocardiograms for control were made before any of the drug had been given, and subsequently every twenty-four hours. Weights in kilos were obtained in the beginning of the experiment. The children were all under similar circumstances. No element was present which might have induced tachycardia, such as fever, excitement or emotion. The drug was given in small amounts of water, at times with small quantities of saccharin, four times daily, when the stomach was more or less empty. The estimated total dose was divided so that an interval of six days was required for the administration of the total amount. The drug was measured out in individual doses in minims, using a minim glass, not a dropping pipette; but the total amount of the drug and all estimations were made in cubic centimeters.

Evidence of the action of the drug was indicated by vomiting or such alterations of the electrocardiograms as have been previously recognized as digitalis effects. The appearance of any of these phenomena was taken as the end-point of the observation and the drug was discontinued. The amount of the drug which had been taken up to this time was estimated to be the dose necessary to produce a therapeutic effect. Vomiting was often associated with

[2] Am. Jour. Pharm., 1910, lxxxii, 360.

malaise and discomfort, but the difficulty in interpreting these latter two symptoms in children made them unsatisfactory to rely upon as positive evidence. The vomiting was considered to be an effect only when it occurred at times other than immediately after the drug was administered and when it could not be attributed to some other cause.

Case No.	Age in months.	Weight in kilos.	No. of c.c. every 4 hrs.	No. of doses received.	Initial and subsequent effects noted.	Total c.c. of drug received.	C.c. per kilo received.
1	13	8.5	1.06	5	Vomiting; partial *A–V* block; increased inversion of *T* III	5.30	0.62
2	25	8.9	0.33	6	Sinus arrhythmia; decrease in ventricular rate	2.00	0.22
3	16	9.1	1.14	7	Vomiting; increase in *P–R* time	8.00	0.88
4	12	9.6	0.80	24	No effects produced	19.20	2.00
5	20	9.6	0.80	12	Sinus arrhythmia; decrease in ventricular rate	9.60	1.00
6	21	9.6	0.80	24	None	19.20	2.00
7	24	9.6	0.67	16	Sinus arrhythmia; decrease in ventricular rate	10.00	1.05
8	28	10.0	1.20	14	Partial *A–V* block; later sino-auricular block; vomiting	16.00	1.60
9	23	11.1	0.90	8	Sinus arrhythmia; decrease in ventricular rate; vomiting	7.20	0.65
10	30	11.2	0.60	10	Decrease in ventricular rate	6.00	0.53
11	24	11.7	0.71	14	Sinus arrhythmia; decrease in ventricular rate; increase in *P–R* time	10.00	0.85
12	34	12.8	1.60	4	Vomiting; sinus arrhythmia	6.40	0.59
13	27	13.3	1.67	12	Vomiting	20.00	1.50
14	49	13.9	1.73	12	Vomiting; sinus arrhythmia	20.80	1.50
15	42	14.4	1.80	14	Vomiting	25.20	1.74
16	48	14.7	0.93	16	Vomiting; increase in *P–R* time	15.00	1.06
17	66	14.7	1.57	7	Sinus arrhythmia; vomiting	11.00	0.75
18	35	15.0	0.53	6	Sinus arrhythmia	3.20	0.21
19	36	16.0	1.33	8	Vomiting; partial *A–V* block	10.70	0.66
20	46	16.0	1.34	5	Vomiting	6.70	0.41
21	62	16.8	1.40	18	Decrease in rate	25.20	1.50
22	72	17.1	2.15	4	Vomiting	8.60	0.50
23	51	17.6	1.47	9	Increase in *P–R* time; vomiting; increased inversion of *T* III	13.20	0.75
24	72	19.0	2.00	8	Sinus arrhythmia	16.00	0.84
25	60	21.0	0.83	23	No effect produced	19.00	0.90
26	96	21.8	0.83	23	No effect produced	19.00	0.87
27	79	23.4	2.98	13	Vomiting; decrease in ventricular rate	38.80	1.66
28	132	26.8	1.67	20	Vomiting; increased inversion of *T* III	33.30	1.25
29	132	27.7	2.16	20	Vomitlng; decrease in ventricular rate	45.20	1.50
30	144	27.7	2.00	24	Increased inversion of *T* III	48.00	1.74
31	120	29.0	0.81	22	No effect produced	18.00	0.62
32	120	30.8	0.81	22	No effect produced	18.00	0.58
33	132	33.0	1.00	24	No effect produced	24.00	0.73
34	156	40.0	1.67	24	No effect produced	40.00	1.00
35	156	40.5	1.13	24	No effect produced	27.00	0.66
36	180	50.0	2.00	24	No effect produced	48.00	0.96

Alterations of the normal electrocardiogram, which were recognized as digitalis effects, are decrease in rate and sinus arrhythmia; prolongation of the auriculoventricular conduction time, sino-auricular and auriculoventricular heart-block, premature ectopic contractions and alterations in the form of the *T* wave.

In this group of cases we have considered a persistent decrease in the rate of fifteen or more beats per minute as counted on the electrocardiogram as positive evidence of digitalis effect. Many of the control curves showed slight variations of the cardiac rhythm, but certain cases developed a very exaggerated sinus arrhythmia which was independent of respiration and which was attributed to digitalis. A few of the cases showed a well-marked sinus arrhythmia in the control curves, and in these cases any further alteration in rate or of this arrhythmia was not considered a digitalis effect. Sino-auricular heart-block was noted. Further changes were prolongation of the *P–R* interval of 0.040 second or more up to partial auriculoventricular block. Diminution in size or reversal of direction of the *T* wave were also observed and attributed to the action of the digitalis.

Discussion. Vomiting was observed as the first sign in 13 cases. When it occurred it seemed to be an early symptom and came after the administration of smaller quantities of the drug than were required to produce the other effects.

The rate was decreased more than fifteen beats per minute in 9 cases. Of these 9 cases, 5 showed a definite sinus arrythmia. The appearance of the sinus arrythmia in these children also seemed to be an early symptom, occurring before other changes in the electrocardiogram took place. The decrease in the rate without a sinus arrhythmia was not an early symptom.

Sinus arrhythmia which had not been present in the control curves appeared in 9 cases, and was well marked in all. In the curves of the sinus arrhythmia it was found that the *P–R* interval showed considerable variation. It was always shortest after the long diastolic pauses and longest during the periods when the rate was increased. When the *P–R* interval was prolonged in these periods of increased rate it was increased beyond the normal *P–R* time as observed in the control curves. An example of this effect is shown in Figs. 1 and 2 from Case 36. They show a sinus arrhythmia not related to respiration. Digitalis effect. *Q–R–S* complex normal, *T* wave upright. Ventricular rate varies, being 55.5 per minute in the periods of retardation, 93.8 per minute in the periods of acceleration. The *P–R* time varies from about 0.120 second after the long diastolic pauses; when the rate increases to 90 the *P–R* time is 0.160 second. The normal ventricular rate in this case was 93.5 per minute. The normal *P–R* time was 0.160 second.

Interpretation. Sinus Arrhythmia. Otherwise Normal Curves. An electrocardiogram similar to No. 3911 (Fig. 1) was obtained.

At 2 P.M. the patient was given 0.001 gram of atropin sulphate intramuscularly. Record No. 3916 was obtained at 2.45 P.M. It shows a normal cardiac mechanism. No evidence of any arrhyth-

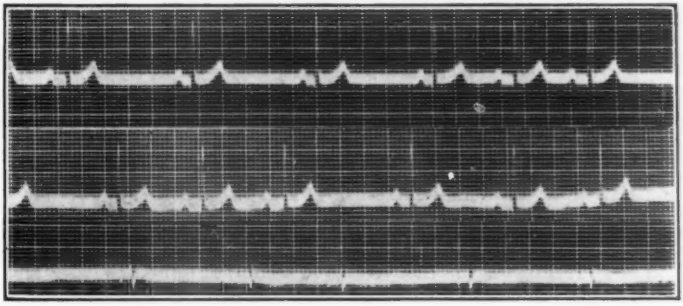


FIG. 1.—Electrocardiogram No. 3911. Made April 8, 1920.[2]

mia. *Q–R–S* complex is normal. The *T* wave is diphasic in Lead I and II, inverted in Lead III. Ventricular rate, 150.0 per minute. *P–R* time, 0.120 second.

Interpretation. Normal cardiac mechanism. Tachycardia due to removal of vagus inhibitory influences. *T* wave inverted.

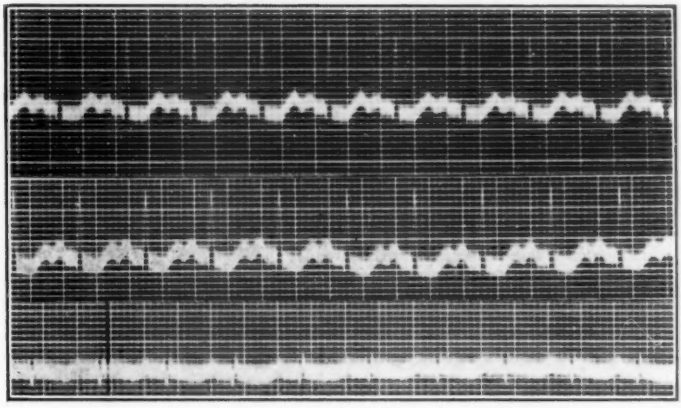


FIG. 2.—Electrocardiogram No. 3916. Made March 9, 1920.

The variation of the *P–R* time in these cases may be explained in two ways: There may be a digitalis effect of the conducting tissue, causing a delay in the passage of the impulse, which may be apparent only when the rate is faster and the conducting tissue has not the

[2] Lead I, II and III from above downward and from left to right. The three usual leads made under standard conditions.

same length of time in which to recover from the fatigue produced by the spread of the preceding impulse. Under such circumstances the *P–R* interval will be longer in the periods of faster rate and will be short in the periods of slowing when the conducting tissue has had sufficient time to recover. Or the variation in the *P–R* interval may be evidence of variations in vagus action in association with fatigue in the conducting tissue, as the vagus nerve on stimulation delays the conduction of the impulse from auricles to ventricles.[4] Removing the vagus influence on the heart by injection of atropin in our cases showed a complete release of the heart from vagus inhibition and a coincident disappearance of the sinus arrhythmia, the *P–R* interval being constant and not prolonged.

Depression of the impulse conduction from the sinus node to the auricles was shown in one case by sino-auricular heart-block.

The *P–R* interval was delayed 0.040 second or more in 4 cases and partial auriculoventricular heart-block occurred in 3 cases.

Alteration in the form of the *T* wave was observed 4 times.

Ten cases showed no sign of digitalis effect. Of these 10 cases 8 were under observation in the beginning of the study when the dose given was too small to produce an effect. The remaining 2, for reasons not apparent to us, showed no reaction after very large doses. It is possible that certain individuals may be unusually tolerant to digitalis given by mouth or may fail to absorb the drug.

In children weighing twenty kilos or less a response was noted in 14 patients with doses below 1 c.c. per kilo, while in only 8 patients was the dose necessary to produce an effect above 1 c.c. per kilo. In children whose weight was above twenty kilos 8 did not respond when the dose of digitalis was below 1 c.c. and 4 responded only when the dose was considerably above 1 c.c. It would seem, then, that children up to the body weight of twenty kilos are somewhat more sensitive to digitalis than children above that weight.

Considering the group as a whole, however, in only 3 patients were digitalis effects noted on doses corresponding to the dosage described by Eggleston as sufficient to produce an optimum therapeutic effect on adults. No effect was noted in 8 patients after doses of 2 or 3 or more times the amount prescribed by Eggleston. Effects were obtained in 13 patients only after administration of doses 2 or 3 times as great and in 10 only with doses at least five times as great. It must be considered that Eggleston's formulæ have been applied to patients with heart disease and not to patients with normal hearts. Administration of quite large amounts to these children was never attended by other than very minor evidences of digitalis action.

Conclusions. 1. Our results show that between eight and twenty kilos of body weight, or up to the approximate age of four years,

[4] Robinson and Draper: Jour. Exper. Med., 1912, xv, 14.

children respond more readily to digitalis than do children above this weight and age. It would seem that older children with normal hearts require a larger amount per unit of body weight than is necessary to produce an effect in adults with heart disease.

2. There is considerable variation in the amount of digitalis necessary to bring about a response in the hearts of children.

3. We have noticed vomiting to be one of the early signs of the effect from digitalis administration, often occurring before there were any alterations in the electrocardiogram. Changes in the electrocardiogram were not constantly found in all the cases in which a digitalis effect was obtained. The most common change observed in this group of children was the appearance of a sinus arrhythmia. Alteration in the size and direction of the *T* wave occurred in a small number of all the cases.

PEDUNCULATED TUBERCULOSIS OF THE PERITONEUM: PERLSUCHT: EXTREME INFREQUENCY OF THE CONDITION IN THE HUMAN: REPORT OF A CASE WITH DISCUSSION OF BOVINE INFECTION.

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In contrast to the types of tuberculosis of the peritoneum and pleura observed in the human, peritoneal and pleural tuberculosis in cattle manifests itself in the production of caseous or calcified masses of variable size, surrounded by a fibrous capsule and embedded in a rather loose proliferating connective tissue distinct from the subperitoneal connective tissue; frequently these masses attain considerable dimensions and by their weight draw out the underlying connective tissue, thus acquiring a pedicle. Practically always there are associated bands of adhesions studded with rows of caseous sessile nodules, suggesting the appearance of a string of pearls, whence the name "Perlsucht." While this type of tuberculosis can be observed *par excellence* in the sheep, it is the form in which tuberculosis of the serous membranes of all cattle most frequently manifests itself.

It is interesting to note that this type of tuberculosis is an exceedingly rare occurrence in the human, there being recorded in the literature the description of but two cases, the first by Bizzozero in 1867 and the second by McCallum in 1901. Bizzozero was unable to find recorded a similar condition, and later McCallum, who included in his thorough investigation of the literature the excellent reviews of the more recent literature of Brunn, failed to find any reference to a similar condition.

The case reported by Bizzozero occurred in a twenty-four-year-old peasant who died with the symptoms of pulmonary tuberculosis. The autopsy revealed conglomerated tubercles in the lungs with cavities in the apices. The peritoneal cavity contained about a liter of seropurulent fluid and the loops of intestine were firmly adherent to one another by a yellowish exudate. Removal of the exudate revealed innumerable whitish, tuberculous nodules of the size of the finest grain of millet seed to that of a pea, scattered throughout the visceral and mesenteric peritoneum. Sometimes the tubercles united to form a plate the size of a five lira piece. The nature of the peritoneal tubercles, especially those of the mesentery, was very varied. Some amounted to mere white spots embedded in the tumefied peritoneum, others projected by their whole height above the level of the peritoneum, while still others were not attached by their point of origin except by a peduncle of a length which varied from 1 mm. to 1 cm. and varying in diameter from 1 to 1.25 mm.; often the peduncle was flattened together, amounting to a thickness of but 0.125 mm. The histologic constitution of the tubercles immersed in the peritoneum and those with the peduncles was the same, and, as usual, had outside a layer of connective tissue in active proliferation and internally the elements in detritus and fatty degeneration. The mucosa of the ileum was pigmented and showed numerous tuberculous ulcers, corresponding with which were especially numerous tubercles on the peritoneum.

"The microscopic examination of the peritoneum," he says, "shows me the probable reason why, while in other cases of tuberculosis the small neoplasms are adherent to the peritoneum, in mine they were for the most part pedunculated. The preparations show that the connective tissues of the membranes were separated by an abundant hyaline fundamental substance in which were numerous new-formed cells, of which some were spherical or oval and others fusiform or stellate; naturally the peritoneum, tumefied and softened by the presence of superfluous fundamental substance and of numerous new-formed cells, could not support the weight of the tubercles, and yielding, formed of necessity a peduncle. The layers of muscle fibers have taken no part in the new formation.

"This case leads me to believe that in all probability tubercles might also produce a kind of free body in the peritoneum, as is the case with fibromata, lipomata, etc., and even sclerosed appendices epiploicæ."

McCallum's case occurred in a white woman, aged thirty-eight years, who died with the symptoms of pulmonary tuberculosis.

At autopsy the peritoneal cavity contained no excess of fluid; the peritoneal surfaces were free and glistening, but lying just under the serous surface of both visceral and parietal peritoneum were numerous nodules which had a most extraordinary arrangement. The

diameters varied from 1 mm. to 2 cm., and while some were only slightly elevated above the level of the peritoneum, most of the nodules hung free, each in a sort of long, blind tube, formed apparently by the drawing out of the peritoneum into a tubular pedicle. Some of the pedicles reached a length of 12 cm. and most of them took their origin from a wide uplifting of the peritoneum. All of the pedicles contained a clear reddish-yellow fluid which could readily be made to gravitate to either extremity by inverting or elevating the distal nodule; in many, the fluid could be made to run back and spread out under the peritoneum of the intestine and perhaps even to enter another tubular pedicle. In a few instances the tubular prolongations showed no caseous mass at the end, and, indeed, one elongated sac with thin delicate walls and clear yellow fluid contents was found entirely free in the peritoneal cavity. In some cases small caseous nodules were found hanging by a stalk inside the elevated peritoneum.

Sections of the nodules showed them to be necrotic except peripherally, where the structure exhibited the characters of tubercosis. Tubercle bacilli were found in great numbers, especially in the zone between the living and necrotic tissue.

The spleen and liver exhibited tubercle-like nodules which proved to have all the histologic features of tuberculosis. The lungs were studded throughout with miliary tubercles, and finally there was a tuberculous leptomeningitis, the pia over the pons, cerebellum and cerebrum showing a yellowish exudate with tubercles along the vessels.

The case which occurred in this hospital was that of a twenty-four-year-old white man, a Polish laborer, who was admitted to the South Side Hospital November 21, 1919, complaining of pain in the chest and abdomen, cough, general weakness and loss of weight. Both the family and previous history were negative. The patient stated that he was apparently well until about five years ago, when he began to suffer with constipation, anorexia and intermittent colicky pains of great severity. Two years ago he began to complain of a hacking cough which persisted to the time of admission. One week before admission he fainted on the street.

Physical examination revealed an emaciated young man, acutely ill and showing marked pallor of the skin with cyanosis of the visible mucous membrane. The thighs were acutely flexed on the abdomen. The chest was of the phthisical type and auscultation revealed many fine and coarse moist rales coming in showers and present all over the chest. Percussion revealed areas of hyperresonance, alternating with areas of dulness. The abdomen was tender and presented a diffuse board-like rigidity. Both ankles were edematous and pitted on pressure. Temperature on admission was 99.6°, rising later to 104°. The pulse registered 140 and was very shallow.

Respirations were 42. Death ensued thirty-six hours after admission.

Autopsy was performed five hours after death, with the following findings:

Anatomic Diagnosis. *Lungs.* Acute hemorrhagic tuberculous bronchopneumonia; chronic ulcerative tuberculosis; chronic productive and adhesive pleuritis (tuberculous).

Heart. Hydropericardium; cardiac hypertrophy and dilatation; acute parenchymatous myocarditis.

Abdomen. Chronic deforming peritonitis with extensive matting together of the viscera.

Gastro-intestinal Tract. Multiple subserous pedunculated nodules of the small and large intestine (approximately 1200 nodules).

Liver. Chronic productive tuberculous perihepatitis; multiple miliary tubercles.

Spleen. Chronic productive tuberculous perisplenitis; multiple miliary tubercles.

Kidneys. Chronic diffuse nephritis (large white kidneys); multiple cortical miliary tubercles.

Résumé of Protocol. The body is that of a poorly developed white male of poor musculature and nutrition, measuring 63 inches long and weighing about 100 pounds. A frothy blood-tinged fluid exudes from both nostrils. The neck is long and narrow and the inferior angle acute. Visible mucous membranes are deeply cyanosed.

The under surface of the recti muscles is intimately adherent to an underlying mass, from which it has to be separated by dissection. This mass is composed of a diffusely thickened and fused peritoneum and omentum, which give rise to an irregularly nodular, grayish yellow and in places caseous material, the whole forming a layer with an average thickness of 2 cm. The nodules in this mass are conglomerated, vary in size, some attaining the dimensions of a hazelnut; they are firm, yellowish gray and apparently free from caseation. This mass fuses with the capsules of the liver and spleen. The intestines present innumerable subserous, pedunculated, whitish yellow, firm nodules which vary in size from a pea to a large hazelnut, and are irregularly globular. In view of the extensive adhesions which wall together all the viscera, it is necessary to dissect out the abdominal and pelvic contents *en bloc*. There is no fluid in the abdominal cavity.

The right pleural cavity presents a few dense adhesions posteriorly; the left pleural cavity is practically obliterated by dense fibrous adhesions. The lungs are voluminous and completely fill the chest cavity. There are multiple irregularly scattered subpleural hemorrhages, some of which attain the size of a quarter. The lungs have a firm, finely nodular feel, cut more readily than normal and pieces sink only slightly below the surface of water. The cut surface is literally peppered with innumerable, regularly disseminated, pin-

head-sized grayish elevations which give to the surface a coarsely granular feel. These are surrounded by a concentric elevated deep reddish zone and then by a depressed brownish-red area. Bases of both lungs are intimately adherent to the domes of the diaphragm, from which they must be cut away. The right lower lobe presents an area of caseation about the size of a quarter. There are no areas of cavitation. Bronchi show a congested and swollen mucosa, to which is adherent a thick, tenacious, bloody mucus. Peribronchial lymph nodes are swollen, juicy and anthracotic.

The liver is intimately adherent to all the adjacent structures and has to be dissected out. Glisson's capsule is greatly thickened, attaining in places 12 mm.; it is grayish yellow in color and firm. The organ, except for its capsule, cuts normally, and the cut surface presents a nutmeg appearance from dilatation and congestion of the central veins. Right lobe superiorly shows on section a small circular pea-sized cavity distended with pus and located about 2 cm. below the surface. There are no tubercles apparent to the naked eye.

The spleen is bound to the adjacent viscera and posterior abdominal wall by dense adhesions; it is enlarged and measures 15 cm. long by 9 cm. wide by 6 cm. thick. The capsule is greatly thickened, attaining in places 9 mm. The substance is soft but non-grumous. The cut surface shows an excess of blood, the Malpighian follicles swollen, and there are numerous reddish-gray, irregularly scattered nodules, the largest the size of a dime and not elevated.

Both kidneys are equally enlarged, measuring 15 cm. long by 8.5 cm. transverse by 6.5 thick. Capsules strip easily, leaving behind a smooth pale cortex in which the stellate veins are congested. There are apparent the persistent shallow grooves of fetal lobulations. The cut surface is distinctly pale, the cortex swollen and the markings indistinct. There are multiple, irregularly scattered, pinhead sized tubercles, all of which are confined to the cortex.

Gastro-intestinal Tract. The coils of the small and large intestine are intimately adherent to each other and to the adjacent viscera. The serosa of both small and large intestine is literally showered with multiple pedunculated, irregularly globular tumor masses, which vary in size, the smaller ones the size of a pea and the largest ones attaining the size of a hazelnut. The pedicles average 3 or 4 mm., are reflected over the nodules and merge into the serosa of the intestine. The nodules proper are grayish yellow, firm and cut with resistance; they are apparently perfectly preserved in the gross and show no central caseation. The cut surfaces are suggestive of fibroma or fibromyoma. The mucosa was carefully examined for evidence of ulceration but was everywhere perfectly intact.

Histopathology. The multiple nodules of the intestine. Numerous sections of these were studied, twenty-four in all. Some of the sections were made through the nodule so as to pass through the

pedicle and underlying tissue. The central portions of the nodules reveal a pale, bluish pink, for the most part homogeneous and in places finely granular substance, which has no definite structure and corresponds to caseous necrosis, notwithstanding the fact that there was no naked eye evidence of caseation. Toward the periphery of the nodules the structure becomes more distinct, presenting the characters of tuberculous granulation tissue, consisting of irregularly arranged epithelioid cells with some multinucleated giant cells and numerous small spheroidal cells; more externally the capsular layer

FIG. 1.—Photograph of intestinal serosa, showing multiple "pedunculated tuberculomas." These were universally distributed over the serosa commencing at the beginning of the jejunum and terminating at the rectum, numbering at least 1200 in all.

is formed by elongated connective-tissue cells over which can be seen in some sections the peritoneal endothelium. There is a distinct demarcation between the tuberculous process in the nodules and the underlying structure of the intestine. The interposed pedicle is composed of a loose, rather vascular connective tissue, showing a sprinkling of small round cells.

Lungs, liver, spleen and kidneys reveal upon microscopic examination numerous irregularly scattered perfectly typical epithelioid tubercles, with areas of caseous necrosis. The parietal peritoneum

shows tuberculous granulation tissue with large areas of caseation, and in places the structure is sufficiently preserved to show the conglomeration of epithelioid tubercles.

Comment.—The type of lesion described in the visceral peritoneum of the foregoing case together with the peritoneal pathology described by Bizzozero and McCallum in their own cases may be explained on a basis of a peculiar and in fact specific reaction of the host to an infection with a tubercle bacillus possessed of a relatively very low grade virulence. The literature on the subject is practically limited to a discussion of the frequency of bovine infection in the

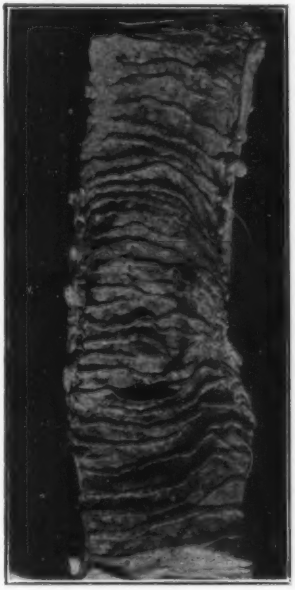

FIG. 2.—Photograph of mucosa of small intestine, showing an entire lack of any evidence of ulceration.

human, its contribution to human mortality and methods of differentiation of the human bacilli from the bovine type. Except for some brief discussion of the human response to bovine infection in the report of the British Commission in 1911, there could not be found in the literature any mention or description of the nature of the pathology in the human resulting from infection with bovine bacilli.

Indeed, the importance of bovine infection in the human, more particularly in children, has been emphasized by Park and Krumwiede, who made an admirable study of 1042 cases with the following

conclusion: "Bovine tuberculosis is practically a negligible factor in adults. It very rarely causes pulmonary tuberculosis or phthisis, which causes the vast majority of deaths in man and is the type of disease responsible for the spread of the virus from man to man. In children, however, the bovine type of tubercle bacillus causes a marked percentage of the cases of cervical adenitis, leading to operation and disfigurement. It causes a larger percentage of the rarer types of alimentary tuberculosis requiring operative interference or, causing the death of the child directly or as a contributing

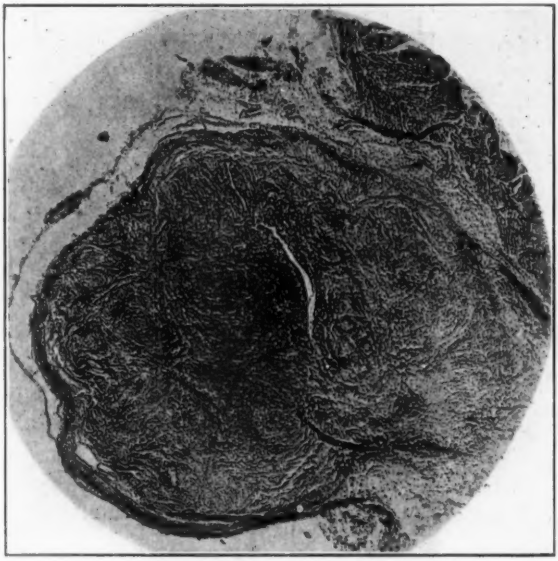

FIG. 3.—Low power photomicrograph of a nodule, showing complete encapsulation with peritoneal endothelium over the capsular layer. Note above and to the right, the muscularis of the intestine separated from the tuberculous process by healthy tissue.

cause in other diseases. In young children it becomes a menace to life and causes from 6 to 8 per cent. of the total fatalities from this disease."

Bacteriologically the differentiation between human and bovine bacilli can be definitely and readily accomplished. Briefly the types are differentiated culturally and by virulence tests as follows: All cultures growing luxuriantly on glycerin egg from the start are of the human type, while those growing sparsely or not at all in the first few generations are of the bovine type. The rabbit or calf virulence test is conclusive; bovine bacilli in every instance when

injected in doses of 0.01 mg. intravenously cause a generalized tuberculosis which is progressive and causes the death of the animal. Human viruses injected in the same amount produce no disease at all or at the most a local tuberculosis somewhere in the body.

It is unfortunate that virulence tests were not carried out with emulsions prepared from the nodules in our case. The immediate impression gained from the gross picture was that of tumor, and, in fact, the subserous nodules were regarded as the intestinal analogy of von Recklinghausen's multiple fibromatosis of the skin, so that

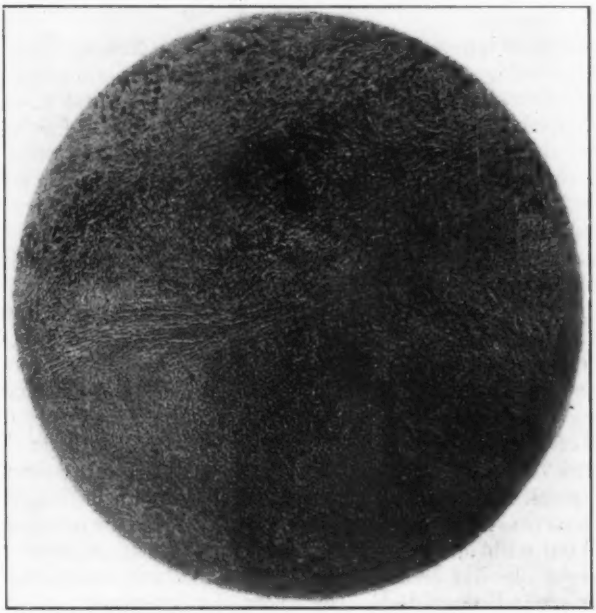

FIG. 4.—High-power photomicrograph taken from low power (Fig. 3), showing caseous necrosis, an epithelioid tubercle and tuberculous granulation tissue.

the specimens were placed in formalin and the tuberculous nature not suspected until revealed by routine histologic examination. The gross pathology of the lesion of our case as well as that of the peritoneum of the other human cases reviewed in this report is in every way identical with the tuberculous lesion of the peritoneum of cattle and designated as Perlsucht. This together with the fact that a very similar pathology has been produced by experimental inoculation of numerous Rhesus monkeys with bovine tubercle bacilli makes it reasonable to assume that the infectious organism in these human cases is very likely of the bovine type. The low-

grade virulence possessed by bovine bacilli for the human, and the established fact that transmutation of one type into another cannot occur, lead to the conclusion that the terminal generalized miliary tuberculosis in the last case was due to a superimposed infection with human bacilli. The British Commission reports two instances in which both human and bovine bacilli were isolated from the same patient, one from a caseous retroperitoneal gland in a seventy-year-old man and the other from a caseous bronchial gland of a four-and-a-half-year-old child dying with generalized tuberculosis. Out of 10 cases of alimentary tuberculosis in children, bovine bacilli were isolated from 4.

Finally it is interesting to call attention to the striking similarity of the pathology in pendulous tuberculosis of the peritoneum and that of the multiple, so-called "sarcoid growths" of the skin, which are grouped by Darier into four types of nodular skin lesions; in three of these the process is almost certainly tuberculous, while the fourth represents probably a form of cutaneous lymphosarcomatosis. As a rule the multiple benign sarcoid growths are characterized by the appearance of rounded, painless nodules which vary in size from a pea to a hazelnut or larger. Histologically the picture is strikingly like that of tuberculosis, variable numbers of giant cells of the Langhans type lying in a stroma of epithelioid and small round cells. While in the group of Boeck ulceration never occurs, the nodules in the second group ulcerate occasionally and are located almost exclusively on the extensor surfaces of the extremities, bearing a clinical resemblance to erythema induratum. In a third group of cases, described by Darier and Roussy as the rarest of all varieties of so-called sarcoid growths, the nodules are rounded or oval, painless, the overlying skin not ulcerated, the individual enlargements vary in size from a pea to a walnut and are occasionally connected with one another by a cordon of easily palpated subcutaneous shot-like bodies. The histologic features as depicted by Darier are indistinguishable from those of tuberculosis.

In many of the reported cases of multiple sarcoids the authors report an associated tuberculosis most commonly of the lungs and lymph nodes. In a second set of cases positive reactions to tuberculin were secured. In still other cases injections into guinea-pigs of emulsified nodules produced typical tuberculous lesions. While at times the reaction in guinea-pigs was prompt, the animal dying in a few weeks, in other instances life was prolonged to the extent of a year or more until sacrifice of the animal resulted in the finding of nodules revealing on histologic examination changes indicative of indolent or even healed tuberculosis, the virulence of the tubercle bacillus thus varying greatly. This latter type of case, together with the cases in which no organisms were found, represent in all likelihood cases of bovine infection which could easily be differen-

tiated by virulence tests in rabbits. Bovine bacilli, while exceedingly virulent for rabbits, practically never cause death in guinea-pigs even when injected in large doses. In this connection it is interesting to note that the British Commission appointed to inquire into the relations of human and animal tuberculosis investigated 54 cases of lupus vulgaris, and in at least 25 per cent. of the cases they isolated tubercle bacilli which corresponded to the bovine type culturally and possessed the characteristic bovine virulence for rabbits.

Summary. 1. A case of pendulous tuberculosis of the peritoneum is reported, preceded by a brief review of the only other two cases of human pedunculated peritoneal tuberculosis recorded in the literature.

2. The condition is compared to the lesion in tuberculosis of the serous membranes of cattle designated as Perlsucht, with which it is pathologically identical.

3. An attempt is made to associate with the process the bovine type of tubercle bacillus and there follows a discussion of the relative virulence and importance of the bovine and human types of tubercle bacilli, in different forms of human tuberculosis, together with a brief review of the methods for differentiation of the two types of bacilli.

4. The pathology is discussed from the standpoint of representing the intestinal equivalent of the multiple benign sarcoids of the skin; in reality, low-grade tuberculous infections, better termed nodular cutaneous tuberculomas.

I wish to express my indebtedness to Dr. Samuel Haythorn, Director of the Singer Memorial Laboratories, for his interest and kindness in making the photographs and photomicrographs.

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THE SEQUELÆ OF EPIDEMIC ENCEPHALITIS.[1]

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At the height of an epidemic the attention of the medical world is focussed on immediate results rather than on after-effects. "Will the patient recover or die?" is the prognostic question above all others. When, however, the fire of the epidemic has burnt itself out and we begin to take stock of the condition of the survivors, other questions press for an answer. "Are certain disabilities to be regarded as temporary or permanent?" "When the patient has made an apparently complete recovery, is all well with him or is anything more to be feared?"

The answer to such questions can already be given in the case of influenza. Many a patient recovers from the disease only to be left a weakling for the rest of his life, open to the attacks of the tubercle bacillus and other invaders of the respiratory tract. What can be said of the recent outbreak of epidemic encephalitis?

In estimating the permanence of the damage done by the virus of epidemic encephalitis it is often difficult to separate what may with justice be called an after-effect from merely a long-continued manifestation of the disease. Sometimes symptoms may persist so long that we may with reason class them as sequelæ. Other after-effects succeed the illness only after an interval of varying duration.

The first cases of the disease appeared in Winnipeg in October, 1919. An analysis of 75 cases personally investigated together with the autopsy findings in 16 cases has been published in previous papers.[1] The worst of the epidemic was over by the end of January, 1920. Sufficient time, therefore, has elapsed to enable some estimate to be made as to the degree of completeness of recovery and to determine whether any untoward after-effects may be expected.

It may be said at once that in our experience complete and rapid recovery is uncommon except in really mild cases, that many patients continue to suffer from some of the symptoms in modified form, and that in a few there appear new symptoms which must be regarded as true after-effects. Of 31 patients who have been communicated with, 20 complained of symptoms after all the acute manifestations of the disease had disappeared.

For convenience of description the symptoms may be divided into four main groups: (1) General; (2) paretic (cranial nerves); (3) irritation; (4) parkinsonian.

[1] Boyd, W.: The Winnipeg Epidemic of Encephalitis Lethargica, Can. Med. Assn. Jour., February, 1920. Epidemic Encephalitis: A Study of Seventy-five Cases with Sixteen Autopsies, Ann. Med., July, 1920.

1. *General Symptoms.* In those recovering from encephalitis perhaps the most common complaint is marked general asthenia, which may last for many months. There is the same lack of energy and initiative so characteristic of the convalescence from influenza, but it is even more marked in degree. A large proportion of the patients reached by our "follow-up" system complained of this asthenia. In some cases it was many months before the patient began to recover strength. One patient was still very weak six months after the onset of the illness.

The explanation of the asthenia is open to doubt. If lethargic encephalitis is regarded as purely an affection of the central nervous system the asthenia may be due to exhaustion of the nerve cells. If, on the other hand, it is a true, systemic infection, with special localization in the central nervous system, as in the writer's opinion is the case, the asthenia may be similar in nature to that following such general infections as influenza and typhoid fever.

Headache, or a sense of fulness or discomfort in the head, has been a common after-effect. It is most frequently occipital in type, but it may involve any region.

Alteration in the temperament has been observed in a number of our cases, sometimes with definite evidence of mental disturbance. One girl, aged six years, after a typical attack of lethargic encephalitis, made a good recovery. Three months later her parents reported that her disposition had undergone a complete change. From being a bright, playful child she had become dull and apathetic and would sit for hours motionless in a chair, almost like one suffering from myxedema. A peculiar feature was an occasional loss of bladder control, more especially at night.

At least three of the cases have developed mental symptoms. In two of these delusions were the most prominent feature. In the third there was a general mental deterioration, accompanied by loss of memory and inability to focus the attention.

One patient, after spending three weeks in the hospital, during which he presented a typical picture of the disease, was discharged as improved. Two weeks later he developed an erythematous rash on the neck, arms and body, which was intensely itchy and lasted for about a week. His subsequent recovery was unusually delayed, and even now, nine months later, he has by no means completely recovered his strength.

Occasionally the apathy and torpor characteristic of the acute stage of the disease establish themselves as apparently permanent features of the patient's mental constitution and the flash and speed of the mind are lost forever. One such case reminds one irresistibly of the description given by the Arab physician Karshish in Browning's poem:

> "He listened not except I spoke to him,
> But folded his two hands and let them talk,
> Watching the flies that buzzed."

Whether the mental processes of such a patient will ever return to normal it is at present impossible to say. It appears not unlikely that he will gradually sink into a state of dementia.

An interesting example of what may be considered as the general after-effects of encephalitis is the following:

Mr. W. K., aged sixty-six years, suffered from a characteristic attack of epidemic encephalitis in November and December, 1919. The outlook for some time was extremely grave, but eventually he made a wonderfully good recovery and was discharged from the hospital just before Christmas. An account of the case, with a photograph of the patient, has already been published. For some time he remained perfectly well and was able to take part in the work of a farm. About a month later, however, he began to experience a weakness which gradually increased until he was no longer able to work. He would wake up in the morning feeling fresh and fit for work, but in the course of half an hour he would be quite exhausted and fit for nothing but to lie down. From being quite alert mentally he again lapsed into an apathetic and sleepy condition, dropping off to sleep at a moment's notice. About the same time he began to suffer from stiffness and "rheumatic pains" in many of his joints. The stiffness of the arms was so pronounced that he was unable to put on his coat. His hands became swollen and puffy and later desquamated. At the time of the original illness diplopia was a prominent symptom. It disappeared with recovery, but with the onset of these fresh symptoms it reappeared, although only at occasional intervals. A humming noise in the ears was also noticed.

When seen by me for the second time, on August 10, 1920, I was at once struck by his dull, heavy, bucolic look, which was much more marked than at the time of discharge. It was not the mask-like face of Parkinson's disease, seen so frequently in these cases. Rather did it remind one of the appearance in myxedema; there was the same yellow tint, the same broad, heavy look, the same puffiness of the face—a condition, indeed, to which the patient himself made reference. Slight weakness and tremors of the left side of the face recalled the facial paralysis on that side from which he had suffered during the initial illness. All the reflexes were normal. There was some desquamation on the chest and on the back of both hands. He was able to converse perfectly rationally, but cerebration was very slow and the memory was defective. He complained of copious salivation and severe constipation.

The general impression produced on the observer was that of a person in whom both the physical and mental peculiarities were due to hypofunctioning of the thyroid. I know of no case recorded in which definite thyroid disease could be attributed to epidemic encephalitis. That such may occur, however, was shown by one case in my own experience. A young woman had previously suffered

from exophthalmic goiter, but for four years she had shown no signs of hyperthyroidism, although presenting a slight degree of exophthalmos. Following an attack of encephalitis, however, the symptoms of hyperthyroidism returned in full force, and she now presents a typical picture of Graves's disease. I greatly regret that in a series of eighteen autopsies on cases of epidemic encephalitis I omitted to examine the condition of the thyroid in every instance.

The case of Mr. K., just recorded, affords a good example of true sequelæ, the consequences of the disease. Occasionally, however, one meets with what appears to be a relapse or recrudescence of the original trouble. Economo[2] reports a remarkably interesting case of this description in which there were several severe attacks, separated by periods of remission. He died two years after the onset of the illness. The brain showed numerous lesions, both recent and old, characteristic of epidemic encephalitis.

One case of this description has occurred in our experience.

Mr. D., aged twenty-seven years, was admitted to the hospital on June 15, 1920. Three days before he was overcome by weakness while at work and the next day was confined to bed. On admission he was in a drowsy, stuporous condition, although restless and excited at night. He was unable to answer questions and did not appear to be conscious of his surroundings. The temperature fluctuated between 101° and 103° for eighteen days, when it returned to normal. About the same time there was marked improvement in both his physical and mental condition. By July 24 he was sitting up in bed and on August 6 he was out on the sun-balcony, bright and cheerful, and apparently well on the road to recovery. About August 16, however, he again began to show signs of physical lethargy and mental torpor. Fever returned, the temperature varying between 100° and 101°. Speech became increasingly difficult and finally he was unable to open his mouth.

When I saw him on August 20 he was lying like a log in bed, flat on his back, with his hands folded across his chest like an effigy on a tomb. Apart from following one about the room with his eyes he showed no sign of life. He was unable to open his mouth or to make any movements except to raise or lower the hand a little way, by means of which he was able to signify yes or no to a question. Cerebration, as judged by such response, was markedly delayed. There was slight facial weakness on the right and distinct ptosis on the left side. The right pupil was larger than the left. Both fundi showed a low grade of neuroretinitis. This process, in the opinion of the ophthalmologist, was early. The most painful stimuli produced no change in the facial expression, but when asked if he felt pain he signified in the affirmative. Both knee-jerks were increased and on the left there was persistent ankle-clonus and a

[2] Economo: Subacute lethargic encephalitis, Wien. Arch. f. inn. Med., June, 1920.

positive Babinski sign. The urine was normal and the cerebrospinal fluid showed a slight increase of globulin. A couple of days later the temperature fell to normal, the ptosis disappeared and he was able to make monosyllabic replies. Apart from this, however, there has been no improvement.

The interest of this case lies in the fact that it is apparently an example of a true relapse. The return of fever, the ptosis, the Babinski sign and the lethargy all suggest a recrudescence of the disease rather than an epiphenomenon developing as a consequence of vascular or other derangement.

A few brief summaries from the "follow-up" records may be given as illustrating the subsequent history of some not unusual cases:

Mr. N. suffered from a severe attack of epidemic encephalitis in December, 1919. It was remarkable for extremely violent myoclonic spasms of the rectus and other abdominal muscles, which continued over a period of several weeks. He made a good recovery. In June, 1920, he says that he feels well except for tiredness, which is worse in the morning and passes off toward the evening. Works in a store about three hours a day and spends the rest of the day lying down. Tremors have all gone. His weight, which before his illness was 145 pounds, is 158 pounds.

Mr. R. Recovered from a severe attack at the beginning of January, 1920. In May he says that he feels "Not too bad and not too good." Complains of "soreness" on the top of the head, in the stomach region and in left thigh. He is now back at work.

Miss L. was discharged from the hospital as "improved" at the end of February, 1920. In June she was still listless and apathetic, with vacant expression and unable to read for more than a few minutes at a time.

Miss K. was discharged from the hospital on December 18, 1919. At first she had presented a picture of acute paralysis agitans, followed later by lethargy and somnolence. In September, 1920, she says that she has never felt well since leaving the hospital. Complains of general weakness, headache, "rheumatic pains" in hip and shoulder and stiffness in ankles and feet. Occasional attacks of well-marked diplopia.

2. *Paretic (Cranial Nerves).* Evidence of prolonged cranial nerve involvement has been observed in a number of cases. In several instances in which facial paralysis was a feature of the disease proper a lingering weakness has been detected many months later. In none of our cases, however, has the paralysis been complete or even pronounced.

Diplopia has been a more common symptom. In some cases it was a feature from the beginning of the illness; in others it came on after an interval of apparent recovery. The mechanism of such recurrence will be discussed later in this paper.

Weakness of accommodation is perhaps the most frequent indication of cranial nerve weakness. For many months patients have been unable to read except with the aid of glasses, and there may be permanent impairment of vision. A marked example of this condition is the following:

A. M., a returned soldier, suffered from a typical attack of epidemic encephalitis in the beginning of December, 1919. When he began to recover from the illness toward the end of the month he found that he was unable to read. With the aid of +3D glasses he could read with perfect ease. A subsequent examination made in August, 1920, showed that no improvement had taken place in the eye condition and that paralysis of accommodation was still complete.

Of the cranial nerves involved the most important is the optic. During the acute stage of the illness optic neuritis is very uncommon. There has not been a single instance in our series, although careful ophthalmoscopic examinations were made in nearly all the cases. In several cases congestion of the vessels and slight haziness of the edges of the disk were noticed. Notwithstanding this absence of evidence of acute inflammation there were at least two cases of undoubted optic atrophy. In one of these there was marked dimness of vision two months after recovery from the acute attack and the patient was unable to distinguish colors at two feet. A marked secondary optic atrophy was found on ophthalmoscopic examination. The second case, seen six months after the onset of the illness, was also marked by great dimness of vision, and the ophthalmologist's report was as follows: "On the right side the pupil is widely dilated, with complete loss of reaction to light. There is a marked degree of optic atrophy. The retina around the disk shows considerable degeneration. Evidently a low-grade inflammatory condition. In the left eye the pupil reacts very slightly to light. There is commencing optic atrophy. The retina around the disk shows the same condition of progressive low-grade chronic inflammation as is seen on the right side. One patch about 1 mm. in diameter just below the disk shows complete degeneration, but the retina all around the disk is partially degenerated and grayish in appearance."

3. *Irritation Group.* The most remarkable of the sequelæ of epidemic encephalitis in the experience both of such observers as of Farquhar Buzzard[3] and of ourselves have been motor disorders of the nature of spasms, automatic, athetoid and choreiform movements. These may merely form a continuation of the clonic movements so frequently observed in encephalitis, and especially affecting the abdominal muscles, or they may arise *de novo* in a patient never previously exhibiting such phenomena.

[3] Encephalitis Lethargica, Proc. Roy. Soc. Med., 1919, No. 9, vol. xii.

The following case is an example remarkable for its extremely long duration and for the fact that there were no intervals or intermissions.

Mr. N., aged twenty-five years, was admitted to the hospital at the beginning of January in a dull and apathetic condition. The temperature was 102°. He lay in bed, staring at the ceiling in a stupid, cow-like fashion. The cerebrospinal fluid was under high pressure, 80 c.c. being withdrawn. The cells and globulin were normal. He soon lost the power of speech, there being actual difficulty in articulation. Although extremely emaciated he exhibited a ravenous appetite and suffered from intense thirst. Despite a marked degree of polyuria, sugar was never present on any occasion. Toward the middle of March tremors began to appear. These were well marked on both sides of the face and about the mouth, and also in the hands and arms, but the left leg only showed slight tremors. The abdominal muscles were not affected. The corners of the mouth were retracted about seventy-five times per minute. The twitchings of the hands were rhythmic, being faster on the left side than on the right. On one day those on the left were 240 and on another 188 per minute. The thumb and fingers of the left hand showed typical cigarette-rolling movements. There were periods of complete rest. The face was frequently bathed in profuse perspiration. The twitchings continued unabated until the patient's death which occurred early in July, six months after the onset of the disease. I did not have an opportunity to examine the brain.

In such a case it is difficult to speak of sequelæ, for the patient never appeared to emerge from the mental stupor characteristic of the onset of his illness. At the same time an interval of ten weeks elapsed before the development of the tremors.

There have been no cases in our series which have developed involuntary movements after an interval of perfect health, as in the many striking cases described by Buzzard. The following case, however, for a description of which I am indebted to Dr. Gordon Bell, affords an interesting example of an automatic action from an imperative idea developing during convalescence.

Mr. M., aged forty-five years, walked into the laboratory, sat down and crossed his right leg over his left. There were a number of people in the room at the time and he was not attended to at once. After sitting perfectly still for a minute he suddenly arose and walked around the room, from left to right, with a gait so peculiar that it is difficult to describe. It had the stiff, automaton-like character of the sentry-go, but in an almost grotesque degree. Having completed the circle he sat down and crossed the right leg over the left, all the time with a face expressionless and inscrutable as the sphinx, save for a peculiar twitching of both upper eyelids. A minute later he repeated the performance, nor did it differ from

the preceding one by a hair's breadth. When taken into an adjoining room and examined he was afraid of being laughed at and explained that he was utterly unable to help himself. He gave a typical history of epidemic encephalitis. Nearly a month ago he was seized one day with weakness in the legs, and on getting up the next morning found that he was unable to shave, as he saw two faces and two razors. The diplopia lasted for a few days and was then replaced by the double facial paralysis, which was still so much in evidence. The entire face was immobile, except for marked tremors and twitchings of the upper lids. A peculiar and interesting symptom was marked parosmia: he was constantly aware of disagreeable smells, and this proved to be the most lasting of his symptoms. At this stage in his recital he jumped to his feet and went through his customary evolution. He then explained that this distressing complication had developed during the period of convalescence, that he was wholly unable to control the impulse and that it was not to relieve any peculiar sensation in the legs, but because of something he felt inside his head, that he was compelled to behave in a manner he felt to be so ridiculous. He put his feet up on the table and vowed that he would stick to his chair, but the flesh proved too weak. The subsequent history was that the patient gradually improved, and in the course of a few months he was free both of his facial paralysis and his distressing automatism. The parosmia, however, still persists.

In a recent paper by Buzzard several examples are given of involuntary movements coming on many months after the initial illness. This illness occurred in one case in May, 1918. In September of the same year the patient noticed involuntary twitching of the right toe, which spread until it affected the greater part of the right leg and right shoulder. In December the right arm displayed spasmodic contractions every one or two seconds, which caused it to be thrown behind the trunk or slightly elevated. Clonic contractions occurred in the muscles of both buttocks and in the right thigh and leg. There were irregular rotatory movements of the abdominal wall and umbilicus. In another case constant movements of both shoulders appeared six months after an attack of epidemic encephalitis; the movements are described as being "trouser hitching" in character. Contractions of several groups of muscles in the legs were observed, and there were also forced movements of the head.

4. *Parkinsonian Group.* Many groups and subdivisions of epidemic encephalitis have been suggested. A long list of these is given in Tilney and Howe's recent monograph.[4] They may all be collected into three great classes, depending upon the brain level mainly involved. These are the upper cerebral or cortical group,

[4] Tilney and Howe: Epidemic Encephalitis, New York, 1920.

comprising a comparatively small number of cases manifesting such symptoms as hemiplegia, hemianopia, spasms and convulsions; the thalamic group with symptoms suggestive of Parkinson's disease; and the brain-stem group in which involvement of such cranial nerves as the oculomotor and facial is often associated with varying degress of somnolence. It is true that the disease process refuses to be confined to water-tight compartments, but for descriptive purposes such a classification is convenient.

In any considerable group of cases of encephalitis many examples of what may be called the Parkinsonian type will be encountered. Our series has provided some striking pictures of paralysis agitans, although without the characteristic tremor. A case described by Russel[5] bore a close resemblance to progressive lenticular degeneration, including the peculiar emotional disturbances. We have observed that such cases are slower in clearing up than are those of any other group. Not only are the symptoms persistent, but it almost appears as if in these cases the lesion were progressive.

A case in point is the following:

Mr. Z., aged twenty-three years, was under observation for nearly a month in the Winnipeg General Hospital suffering from epidemic encephalitis. At the commencement of his illness the chief features were restlessness and insomnia, but these were soon replaced by marked lethargy and drowsiness. The face acquired the mask-like appearance of Parkinson's disease, and when he was able to be up the posture and gait were also suggestive of that condition. He made a fairly good recovery, but even on discharge his face lacked that play of emotional light and shade which distinguishes the normal individual. When seen eight months later he was markedly worse. Some progressive lesion had apparently been at work. He sat leaning forward in his chair with the blank, expressionless face of a mask. He walked with a shuffling gait, the back bent forward, the arms flexed at the elbow and the hands at the wrist, the rigid gaze fixed on the ground. He had been unable to work for some months and there was a considerable degree of mental impairment. The pupils did not react to light, and the optic atrophy and retinal degeneration already described in an earlier section were observed on ophthalmoscopic examination. The picture presented was one of Parkinson's disease without the tremor.

In the next case the patient never completely recovered his health. At the same time the Parkinsonian features did not develop for some months, so that they may with justice be regarded as true sequelæ. For the details of this case I am indebted to Dr. A. T. Mathers.

Mr. M., aged sixty-two years of age, at the beginning of January, 1920, began to see double and suffered from insomnia, but later

[5] A Study on Epidemic Encephalitis, Based on the Study of Seventeen Cases with Two Autopsies, Canada Med. Assn. Jour., August, 1920.

became very lethargic and drowsy. He was in bed for three weeks and has not been well since. At the present time (September, 1920) he complains of constant headache, of a feeling of dizziness or light-headedness, of clumsiness of the right side of the body and of an increased secretion of saliva. The face is immobile and expressionless. The gait is clumsy and he sways slightly as he walks. The right arm hangs as if useless and can only be used clumsily, but is not deficient in power. The right leg shares in the clumsiness. There is slight rigidity of the muscles on the right side of the body and the deep reflexes on that side are distinctly exaggerated. Adiadokokinesia and asynergia are marked on the right side. Vision is failing rapidly and ophthalmoscopic examination shows indistinctness of the margins of both disks, which are redder than they should be and are covered with numerous small vessels. The cerebrospinal fluid shows a slight increase in globulin, but is otherwise normal.

Tilney and Howe describe a case very similar to the above: Ten months previously their patient had suffered from an acute illness associated with dulness, stupidity and somnolence. A few weeks later paralysis of accommodation developed, together with weakness of the right side of the face and tongue, and the right arm and leg. On examination marked clumsiness and stiffness of the right arm and hand were observed, and to a lesser degree of the right leg. There was paresis of the right side of the face and tongue. The condition is described as hemilateral paralysis agitans without tremor.

In our own case two elements may be distinguished, the thalamic and the cerebellar. A lesion in the hypothalamus involving nerve paths running from the red nucleus through the superior cerebellar peduncle to the dentate nucleus of the cerebellum might account for all the symptoms.

The mechanism by which the sequelæ are produced may now be considered briefly: In order to form a conception of what may occur it is essential to have a clear picture of the condition of the brain when the acute attack is over. The brain substance has been the seat of an inflammatory process, the brunt of which has fallen not on the nerve cells but on the interstitial tissue. An inflammatory exudate has been formed, mainly perivascular in type, but also extending into the surrounding brain substance, and in the more severe cases hemorrhage and thrombosis are present, accompanied by a corresponding degree of tissue disintegration and degeneration. Such a condition in any other part of the body would be followed by organization and repair, with fibrosis, and in the brain fibrosis when once started is by no means a self-limited process.

The net result of all this is interference with nerve paths. Positive symptoms, as Hughlings Jackson long ago pointed out, cannot be produced merely by negative or destructive lesions, and must be attributed to the uncontrolled action of nervous impulses normally

held in check. It is probable that many of the involuntary and spasmodic movements may be traced to the overaction of primitive motor paths arising in the thalamic region, just as similar movements in progressive lenticular degeneration are due to lesions in the lenticular nucleus.

To one familiar with the microscopic picture in any large series of cases of epidemic encephalitis the wonder is not that after-effects are common, but that, to any marked degree at least, they are comparatively rare. We cannot leave the uncertain ground of hypothesis until more observations have been made on the condition of the brain in encephalitis after a considerable interval has elapsed. Greenfield[6] has described extensive calcification of the vessels in a case which died four months after the acute illness. Should such an occurrence be shown to be frequent, it is an observation of great importance.

Little is to be gained, however, by idle speculation until a greater mass of pathologic evidence is available, and the future will no doubt shed fresh light both on the clinical manifestations of the disease and on the pathological changes which form their substratum.

I am greatly indebted to Dr. F. C. Bell, director of records in the Winnipeg General Hospital, for assistance in tracing the after-history of many of the patients in that institution.

MECHANISM OF LOWERED RESISTANCE FOLLOWING EXPOSURE TO LOWERED TEMPERATURE.

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The following study was undertaken for the purpose of ascertaining if possible the functional and structural changes which follow chilling of the body surface and which lead directly or indirectly to disease. The belief has long been held by clinicians and investigators that when the surface of the body is chilled, certain of the internal organs, particularly the respiratory organs, become more susceptible to bacterial invasion. Other authors, after careful investigation, have reached the conclusion that exposure to lowered temperature, of and by itself, may be a complete cause of disease without the intermediation of bacteria. It was therefore planned to subject an animal to sudden and severe lowered temperature and to take note of alterations of function or structure, with special reference to the possibility of increased susceptibility to zymotic disease.

[6] Buzzard, E. Farquhar, and Greenfield, J. G.: Lethargic Encephalitis; its Sequelæ and Morbid Anatomy, Brain, 1919, xlii, 305.

Ruheman[1] recapitulated the various theories accounting for the deleterious effects of exposure to lowered temperature while he advocated the view that the lowered temperature in some way favored the growth of germs in the body. Lassar,[2] Rosenthal,[3] Fodor,[4] Edelheit[5] and Siegel[6] maintained that lowered temperature itself may cause disease without the participation of bacteria. Siegel presented forceful arguments in favor of this view. Descriptions of the specific changes in function and structure brought about in the different organs by exposure to lowered temperature have been published by various authors. Herz[7] described a local rise in blood-pressure following chilling of a part. Van Oarat[8] noted a rise of 10 mm. Hg in blood-pressure of chilled men. Mudd and Grant[9] refer to a general rise of blood-pressure in chilled animals. Their experiments prove that chilling of the body surface causes constriction of the vessels in skin and mucous membrane. They give a good discussion of the entire subject from the modern standpoint. Rossbach and Aschenbrandt[10] reported that cracked ice applied to the belly of cats caused first a pallor and then a redness of the tracheal mucosa.

Tirelli[11] found in the human subject a leukopenia which lasted seven hours after chilling, but he never found a subsequent hyperleukocytosis. Baecchi[12] working with rabbits found that death from cold was not due to changes in the blood, which he stated were relatively unimportant. Lassar[2] and Siegel,[6] working with rabbits, found that albuminuria followed chilling. Fria[13] and Picci[14] found a similar state of affairs in man. Congestion and petechiæ in internal organs of animals were described by Beck,[15] Lassar,[2] Zillessen,[16] Della Rovere[17] and Siegel.[6] Baro[18] and Stonesco[19] described similar changes as a postmortem finding in persons frozen to death. Stonesco states that gastric petechiæ constitute the most constant and characteristic sign of death from freezing.

In the present series of experiments, rabbits were subjected to generalized lowered temperature in the form of the ice bath at 1° C. For localized applications CO_2 snow was used over certain portions of the surface of the body. During the progress of the experiments, blood-pressure tracings were made by means of a mercury manometer connected up with the carotid under cocain anesthesia. The red and white blood cells were counted before, during and after the cold applications. The urine was examined before, immediately after and at varying intervals after the chilling. Finally, the sixty-eight animals constituting the series were killed and autopsied either immediately after the chilling or at varying intervals thereafter and the gross and microscopic changes noted. For various reasons, principally because the scope of the experiments was modified from time to time, not all the data were collected from all the animals.

The skin of rabbits in the ice bath is first pale and later red.

During the first fifteen minutes of the ice bath the ear veins are so contracted that blood for examination is obtained with difficulty. An hour after the cessation of the ice bath the ear veins are relaxed almost to the point of paralysis, but blood does not even then flow freely from a needle puncture, apparently because tonus is practically absent and intravenous pressure almost zero.

The blood-pressure of the rabbits is usually about 100 mm. Hg, but when suspended in the upright position the rabbit may suffer from a mild degree of shock accompanied by an arterial blood-pressure of 40 to 80 mm. Hg. When the animals are immersed in cold water the blood-pressure rises and remains consistently higher than normal until the animals' vital powers begin to become exhausted, then gradually declines.

Table I shows the blood-pressure in 6 cases. In these cases the average rise in blood-pressure occasioned by the ice bath was 63 per cent. Local applications of CO_2 snow did not cause a rise in blood-pressure.

TABLE I.

Figures represent blood-pressure in millimeters of mercury. The number of minutes refers to the time elapsed since the animal was immersed in the ice bath.

No. of rabbits.	Before ice bath, mm.	After 2 minutes, mm.	After 15 minutes, mm.	After 30 minutes, mm.	After 45 minutes, mm.
79	80	120			
82	80	100	90	88	90
83	55	100	106		
86	43	72	80	80	
88	32	84	100	80	
91	110	130	138		
99	66	100	100	95	

The leukocytes were counted in seventeen animals chilled by the ice bath. Of these all showed a leukopenia at some time within the first hour after the ice bath, which lasted usually about twenty minutes. The leukopenia was extreme in about half the cases, the white cells numbering less than 3000 per cubic millimeter. In seven of seventeen animals, the number of leukocytes in the shed peripheral blood was increased temporarily during the ice bath. The increase was not marked, averaging 40 per cent. The blood in these cases was taken from the ear vein in all but one case in which the blood was taken from the carotid. The results in that case indicated that a uniform method is preferable.

The red cells were counted in six chilled animals and the count was found to be unaffected by the chilling.

In this series all the six animals chilled and kept overnight showed marked albuminuria, but the result was partly vitiated by the fact that of 35 normal animals, 14 showed albuminuria (ignoring "trace" of albumin cases). Of the 6 animals exposed to the ice bath 4 showed

normal urine, free of albumin, before the ice bath, and these as well as the remaining 2 showed either a profuse amount of albumin or a "heavy cloud" of albumin after the ice bath.

This corroborates the current view that external cold exerts an irritating influence on the kidneys. Haidenhain[20] had reported renal ischemia as a result of cold applications to the body surface. It appears likely that vasomotor effects constitute one of the early signs of renal irritation from cold.

Grossly and microscopically the kidneys of the rabbits in this series of experiments failed to manifest any signs of damage recognizable by the methods employed.

Either immediately after the ice bath or at chosen intervals thereafter the animals were sacrificed by a blow on the head and immediately autopsied. The brain and its coverings was examined only once, with negative results. The trachea and abdominal and thoracic organs were examined grossly in all 69 animals. Sections were usually made of liver, lung, spleen, kidney and trachea. Two colons were sectioned for microscopic examination. Pronounced alterations were observed in the lung, stomach and spleen, while the heart, liver, kidney, bowels and other organs were apparently unaffected by chilling. The trachea was variable in its behavior.

Owing to the interesting experiments reported by Rossbach and Aschenbrandt[19] and referred to above, the trachea was examined with much interest. In rabbits subjected to the ice bath and autopsied soon afterward the trachea showed marked variations in different cases. It appears plain that the blood supply of the trachea fluctuates on slight provocation. Table II shows the number of cases presenting congestion of the tracheal mucosa at autopsy. There is marked variability both in chilled animals and in control animals.

In view of the detailed description given by Rossbach and Aschenbrandt it appears altogether likely that under proper conditions the pallor followed by redness which they reported could be produced. The present writer tried to repeat their experiments (with cats) but found that the violence inflicted upon the trachea while slitting it open for inspection was sufficient without hot or cold applications to cause early marked congestion.

An interesting experiment was performed by taking two apparently similar rabbits of the same litter: To the belly of one ice was applied; the other was not handled, and hence was a normal control. After twenty-five minutes the animals were killed in turn, and the trachea of each removed within two and a half minutes. The trachea of the one whose belly was chilled showed marked congestion of the tracheal mucosa; the control animal showed normal tracheal mucosa. Unquestionably the tracheal circulation has a most delicate susceptibility to external influences.

TABLE II.—TRACHEA.

	Trachea congested or cyanotic.	Trachea not congested or cyanotic.	Total.
Experimental treatment accorded animal:			
Chilled in ice bath	12	14	26
Applications of CO_2 to skin	2	2	4
Transfused	2	5	7
Normal animals	1	5	6
Miscellaneous conditions, adrenalin, pilocarpin, injuries, diarrhea, etc.	5	3	8
Effect of Postmortem Changes.			
Animals autopsied more than one hour after death	9	2	11

In the present series of experiments the frequent occurrence of ecchymoses, not only beneath the pleural surfaces but permeating the entire substance of the lung, occasioned surprise by their striking appearance and by their early advent, they having occurred within fifteen minutes after the beginning of the ice bath. The splotches were of the color of oxyhemoglobin, and often the background, constituted by relatively unaffected lung tissue, appeared almost milk white. The splotches of ecchymosis or suggillation occasionally occupied one lobe or part of a lobe of one lung. More often the bases of both lungs were affected, while in one case both lungs were the seat (throughout their entire extent) of multiple small hemorrhagic areas which marked off on the surface the outline of the ribs but which scattered throughout the deeper substance of the lungs after an indiscriminate fashion.

Table III shows the frequency of ecchymosis of lungs in chilled and unchilled animals.

TABLE III.—LUNGS.

	Lungs. ecchymosed.	Lungs not ecchymosed.	Total.
Animals chilled in ice bath	20	13	33
Animals receiving CO_2 snow applications		10	10
Animals transfused	2	4	6
Miscellaneous group, consisting of normal controls; animals found dead in cage; animals dying before experimental chilling was effected; animals receiving adrenalin and pilocarpin; animals depilated with BaS and not otherwise handled	3	16	19
			68

It will be observed that ecchymosis of the lungs may occur from causes other than chilling and that the application of CO_2 snow to the abdomen and hindermost portion of the body did not cause lung changes in any of the ten rabbits studied.

Microscopically the ecchymosed tissue shows many interstitial hemorrhages of capillary dimensions. Usually the hemorrhage does not penetrate the lumen of the alveoli but remains imprisoned in the alveolar wall. Certain areas can be found, however, where the blood has burst into the lumina of the alveoli and trickled into the smaller bronchi. A striking feature is the great number of apparently independent small hemorrhages. Desquamated epithelial cells in the alveoli are rare, and there is little desquamation even in the bronchi.

In the lungs of animals chilled in the ice bath and surviving eighteen hours or more a moderate infiltration of polymorphonuclear leukocytes is seen in the alveolar wall. Lungs of freshly chilled animals do not manifest this.

The stomach was of all organs the seat of the most characteristic changes in the rabbits autopsied. Those animals killed immediately after the ice bath, which usually lasted from twenty to thirty minutes, showed practically no changes in the stomach, but those which survived more than six hours generally showed at autopsy multiple petechiæ just beneath the stomach mucosa. Usually there were from 12 to 100 of these petechiæ.

Table IV shows the relative frequency of occurrence of gastric petechiæ in animals subjected to the ice bath as compared with animals subjected to CO_2 snow applications and unchilled animals.

TABLE IV.—STOMACH.

	Petechiæ in stomach.	No petechiæ in stomach.	Total.
Experimental treatment accorded animal:			
Chilled in ice bath, death within one hour afterward	1	8	9
Chilled in ice bath, death within six to twelve hours afterward	5	0	5
Chilled in ice bath, death within twenty-four hours afterward	4	1	5
Chilled with CO_2 snow, death within one hour afterward	1	2	3
Chilled with CO_2 snow, death within forty-eight hours afterward	6	..	6
Unchilled, death from whatever cause	0	17	17
Chilled and kept over six hours before death	15	1	16
Unchilled, or if chilled, killed within an hour (recapitulation)	2	27	29

Table IV shows that gastric petechiæ occur almost uniformly after applications of CO_2 snow, but this is to be discounted on account of the local effect of the CO_2 snow acting directly through the abdominal wall upon the underlying stomach. No experiments were tried to ascertain whether applying CO_2 snow to remote parts of the body would cause gastric petechiæ.

Table VI emphasizes the fact that several hours had usually elapsed between the ice bath and the animal's death, in all cases

showing gastric petechiæ; and conversely, that normal stomachs were usually found in animals autopsied immediately after the ice bath.

No microscopic studies were made of the stomach. The petechiæ often had the appearance of little globes of blood so near the surface that it seemed almost possible to wipe them off with gauze. They were slightly larger than mustard seeds and withstood gentle friction under the hydrant. In animals kept overnight some of the petechiæ seemed to have been digested away, leaving small punched-out ulcers surrounded by a rosy areola.

The application of CO_2 snow to the surface of the abdomen caused hemorrhagic necrotic areas in the underlying coils of the colon, with ulceration of the mucosa. Vascular injection occurred in the serous coat of the colon. In some instances the gastric mucosa also exhibited areas of diffuse hemorrhage into the mucosa of that part of the stomach lying immediately beneath the point where the CO_2 snow was applied. The serous surface of the stomach lying between the chilling agent and the lesion in the mucosa appeared normal in some of these instances.

The spleen appeared contracted and pale in 8 of 9 animals autopsied just after the ice bath, while in 5 of 9 animals surviving several hours after the ice bath it was swollen and cyanotic. Table V shows the number of cases in which contracted or swollen spleen was observed.

TABLE V.—SPLEEN.

	Spleen contracted, pale.	Spleen normal.	Spleen swollen, cyanotic.	Total.
Experimental treatment accorded rabbit:				
Ice bath, death within one hour afterward	8	1	..	9
Ice bath, death six to ten hours afterward	1	1	2	4
Ice bath, death next day	..	2	3	5
CO_2 snow applied locally, death immediately afterward	..	1	1	2
CO_2 snow applied locally, death next day	..	4	2	6
Normal animal	..	7	1	8
Diarrheic animal	1	1	1	3
Transfused animal	..	2	1	3
Adrenalin administered	1	..	..	1
	11	19	11	41

Discussion. The outstanding fact pervading the results reported above is the intensity of the vasomotor reactions set up by the ice bath and their universal spread over the body. The hemorrhages in the lungs and in the stomach have been explained as infarcts, but infarcts are themselves of such an elusive character that in all probability no profit is to be derived from introducing them into the discussion. Moreover, simple asynchronism of the different

component parts of the blood channels is sufficient to explain these hemorrhages. It seems probable that a delicate adjustment is necessary in order that the blood may pass from the strong-walled arteries into the delicate capillaries without rupturing the latter. Whenever a powerful stimulus is applied to certain blood channels, either their immediate contraction or their subsequent relaxation may so alter the relations between artery, capillary and vein that excessive pressure is brought to bear on certain weak points and rupture results. Undoubtedly the possibility of thrombi must be admitted, but it is not only unnecessary to invoke thrombi and infarction to explain the lesions, but the rapid development of the lesions and the deliberate nature of platelet deposition render such a view difficult to accept.

Blood distribution was found altered in the lungs, the skin, tracheal mucosa, the stomach and the spleen, while others have reported anemia of the kidneys. The alteration in the number of leukocytes in the peripheral blood is probably based to some extent on vasomotor changes.

In order to explain the increased susceptibility to bacterial invasion which follows exposure to lowered temperature the following hypothesis is advanced:

1. That vasomotor tone and organ function are maintained by the successive functionation of different shifts or relays of cells, each having its own threshold of susceptibility to stimulation, and rehearsing its stereotyped function according to the laws of fatigue and its own individual needs.

2. That vasomotor changes exert a provocative or stimulating influence on tissue cells, causing an increase in function.

3. That early though fully developed inflammation with all the classic symptoms is to be explained as excessive liberation of cell function, and that this may lead later to exhaustion, lack of coördination and the consequence of these.

4. That the cell tends to summate the various similar and dissimilar stimuli playing upon it at each given instant and react to its environment as a whole.

5. That the vasomotor changes set up by lowered temperature can be summated with the stimulation from relatively harmless bacteria so as to bring on an excessive liberation of function constituting an inflammation of the affected part.

The reversible nature of the vasomotor changes observed in these animals is worthy of consideration. The skin is at first pale, later red; the tracheal mucosa was found pale or red and the observations of Mudd and Grant[9] indicate that the pallor precedes the redness. Since they contemplate inflammation of the mucosa as a possible result of their experiments, they by implication infer that a red stage is to follow the pale, although they do not confirm Rossbach and Aschenbrandt's[10] observation that the pallor rapidly gives way to

redness. After chilling the spleen is first pale and contracted; later, swollen and presumably congested. Haidenhain[20] observed that the kidney becomes pale during chilling, and while his experiments did not extend to the red stage, still it is likely that this organ, like others, undergoes a reversal.

A similar reversal was found by the author[21] in all of a series of several hundred skin injuries of the proper degree, and it is well known that Raynaud's disease and dermographism are characterized by such a reversal of color.

The universal distribution of this phenomenon is apparently based on the nature of the vasomotor mechanism. The author has recently published the result of experiments supporting the view that the specialized cells of the body tend to react in one stereotyped fashion to all forms of stimuli.[21] The contractile elements of the vasomotor system react by contraction when disturbed—that is, stimulated in any way. This accounts for the first or pale stage referred to above. There is only a certain amount of contractile energy available for each unit of time (with a uniform rate of stimulation), and if a sharp stimulus is applied in such a manner as to make an overdraft on the contractile mechanism during one unit of time, then the supply of contractile energy will fail in some subsequent unit of time after the extra stimulation has subsided. This will bring on the reversed or red stage referred to above.

It seems that not a great deal of attention has been given to the question whether arterial tonus is maintained by the simultaneous contraction of all the smooth muscle fibers concerned or by the successive contraction of different relays or shifts of fibers. The bulk of the evidence favors the latter view. In the case of an arteriole too small to pulsate the practically uniform tonus kept up throughout the day (if not during the night also) could not be maintained by all the cells contracting continuously unless repair and work could proceed in a cell at one and the same time. If it be supposed that the smooth muscle fibers contract successively by shifts this difficulty would be obviated. Pratt[22] has shown that neighboring individual striped muscle fibers do not have thresholds of the same level, but each fiber has its own level of susceptibility to stimulation, and therefore all the fibers do not participate in each contraction of the muscle. Such a state of affairs seems probable in smooth muscle and provides for the individual biologic needs of the fiber as well as for the organic needs of the organism as a whole.

Certain rhythmic and vermicular movements, best illustrated by the heart or the intestine, indicate that contraction of one muscle fiber tends to provoke contraction of its neighbor. Howell described a kind of primitive conductivity which characterizes all protoplasm. This quality tends to cause the transmission of any disturbance in cell life. It may well be supposed that the frank vasomotor fluctuations described in the foregoing experiments would

have an influence on all the cells of the given tissue, and this influence would be of a stimulating nature, for the cells tend to react toward any foreign influence by rehearsing their stereotyped function. The fact that cells tend thus to react has been referred to above. It is true that some cells are subject to inhibition when affected by certain outside influences, but the agents producing inhibition are relatively rare and of a highly specialized nature. (Sherrington has recorded that certain inhibitory reflexes affecting voluntary muscle are reversed by strychnin. This fact is noted to show that the process of inhibition is a highly specialized one.)

The rehearsal of its full stereotyped function on the part of any cell exerts a certain provocative influence on neighboring or related cells, and this influence need not be limited to the same type of cell, but muscle fibers could apparently affect secretory cells, and *vice versa*.

It is well known that depriving the highly specialized cells of blood very soon produces serious damage. It is not to be supposed that ischemia, even of short duration, would be without effect on the cells of the part. Repeated vasomotor spasms in Raynaud's disease eventually lead to death of the part, even though the affected regions, such as the extremities, possess a high degree of resistance.

As further evidence of the provocative effect of vasomotor abnormalities, it may be stated that hyperemia of the mucous membrane is generally accompanied by catarrh. Even angioneurotic edema is often associated with itching, showing that the disturbed circulation of the part provokes hyperesthesia.

Jankowsky[23] pointed out the fact that in the dermographic lesion the smooth muscle fibers have a lower threshold than the secretory cells, and hence a mild stimulus may provoke a response from the local vasomotor apparatus while not affecting the secretory apparatus. The experiments previously referred to have shown that the dermographic lesion is in all respects analogous to the reaction of normal skin toward various irritants and that it shows the same sequence and arrangement of pallor and redness. That is to say, any irritant, mechanical, chemical or electric when of the proper grade tends to provoke the equivalent of dermographism.

The dermographic lesion is inflammation of the purest type, because almost uncomplicated by any injury to the tissues from without. Consequently the dermographic lesion illustrates plainly the stereotyped nature of inflammation, the fact that it begins as a rehearsal of function up to the full capacity of the tissue, the fact that it tends to spread beyond the extent of the actual offending agent. In short that inflammation is really a liberation of functional energy leading quickly to exhaustion. While inflammation is often inaugurated by a foreign agent it may spread by the provocative action of one body cell toward another.

The fully developed early stages of inflammation, including all the classic symptoms, can be explained as simultaneous or synchronized function on the part of all the cells of the part. Inflammation has long been defined as "the reaction to injury." An injury would apparently be any stimulus of sufficient intensity to provoke the five symptoms which in the aggregate we term inflammation. This conception clearly implies that an injury and a stimulus differ only in degree, and since the whole is greater than any of its parts it follows that an injury must be a kind of super-stimulus.

If chemical stimulation alone were the only kind of stimulation causing inflammation it might seem that actual structural alteration of the cells took place in each instance over and above discharge of function, and that these alterations characterized inflammation. It seems highly improbable, however, that all varieties of chemical irritation should give rise to the same structural alteration, or that heat, cold, mechanical violence and electricity should also bring about the same structural alterations. It appears more probable that any structural alterations caused by the various injurious agents would be in each instance characteristic of the agent applied. Consequently they would vary one from another and would not form a part of the constant and uniform picture which we call inflammation. This makes it probable that the essential characteristic of inflammation is simply the state of excessive functionation.

It should be noted that neural stimulation is highly selective and does not ordinarily have the power to provoke full function on the part of both parenchymatous and stroma cells.

The phrase "summation of stimuli" is usually employed to designate a series of similar stimuli, but it is here applied to the similar or dissimilar stimuli, which affect a cell at any moment. Many physiologic phenomena appear to be based on the summation of dissimilar stimuli; among others, the knee-jerk. Without the tonic nerve impulses passing constantly from the cord, mechanical stimulation of the patellar tendon fails to provoke a response. Another example is the explosion of contractile energy set off in the strychninized animal by mechanic stimulation. The irritant effect of the strychnin apparently shows itself in two ways: (1) By causing a series of individual motor impulses, thereby increasing muscle tone, and (2) by stimulating a great number of motor cells subminimally, so they discharge their motor impulses only when an additional (mechanical) stimulus is applied. A third example of summation of dissimilar stimuli is seen when the muscles of a swimmer undergo cramp. In this instance the stimulation due to fright and lowered temperature when summated with the voluntary nerve impulses is sufficient to provoke spasm.

In short the cell seems to be a unit constructed so as to receive stimulation in various ways and to respond in a single way, that is, by a rehearsal of its stereotyped function.

Whatever the normal defences of the tissues against germs may consist of, it seems probable that they would be disorganized by the vasomotor fluctuation brought about by chilling the surface of the body. The deleterious effects of bacteria depend on their mechanical and chemical effect on the tissues. The foregoing paragraphs relating to the provocative effect of vasomotor fluctuations, together with those paragraphs relating to the process of summation of stimuli, suffice to show how chilling the body surface tends to favor bacterial disease.

We know that the bacteria are capable of thriving in inflamed tissues. The connective-tissue cells of the body seem to respond to stimulation by propagation. It is possible that bacteria have the quality of altering their behavior in response to changes in their environment and their response might take the form of propagation, but this subject has not been investigated.

Summary and Conclusions. 1. The changes provoked in rabbits by the ice bath are as follows:

Multiple minute hemorrhages in the lungs.
Multiple minute hemorrhages in the stomach.
Changes in blood content of tracheal mucosa.
Contraction followed by congestion of the spleen.
Pallor followed by redness of the skin.
Albuminuria.
Leukopenia followed by leukocytosis in the peripheral blood.

2. The first five of these changes are apparently caused by vasomotor variation. The remaining two are closely related to vasomotor function.

3. The following hypothesis is offered in explanation of the increased susceptibility to bacterial invasion brought about by chilling the body surface;

a. That vasomotor tone and organ function are maintained by the successive functionation of different shifts or relays of cells, each having its own threshold of susceptibility to stimulation and rehearsing its stereotyped function according to the laws of fatigue and its own individual needs;

b. That vasomotor changes exert a provocative or stimulating effect on tissue cells, causing an increased discharge of function;

c. That early though fully developed inflammation with all the classic symptoms is to be explained as excessive liberation of cell function, and this may lead later to exhaustion, incoördination and the consequences of these;

d. That the cell tends to summate the various similar and dissimilar stimuli playing upon it at each given instant and react to its environment as a whole;

e. That the vasomotor changes set up by lowered temperature can be summated with the stimulation from relatively harmless bacteria, so as to bring on an excessive liberation of function constituting an inflammation of the affected part.

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THERAPEUTIC PNEUMOTHORAX COMPLICATED BY HYDROPNEUMOTHORAX AND PLEURISY, WITH EFFUSION ON THE UNTREATED SIDE. REPORT OF A CASE.

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The coexistence of bilateral pleurisy with effusion is one of the rarest complications in pulmonary tuberculosis. The literature on the subject discloses so few authentic instances that when bilateral effusions are detected their tuberculous origin is seriously questioned. We are still in the dark as to the probable explanation of this phenomenon, but the fact remains that when a patient has a pleural effusion of tuberculous origin on one side he is immune, for a time at least, to pleurisy with effusion on the other.

It is not different in the case of therapeutic pneumothorax whether or not complicated by hydropneumothorax. Once a pneumothorax is induced the patient acquires an immunity f om pleurisy with effusion on the untreated side. Forlanini, who has probably had the widest experience with therapeutic pneumothorax, has never met with a case of hydropneumothorax complicated by pleurisy with effusion on the untreated side. Brauer and Spengler,[1] in their

[1] Handbuch der Tuberculose, 1919, iii, 227.

recent study of pneumothorax, state that there is no record of such a case in medical literature. Among the many hundreds of cases he has treated with therapeutic pneumothorax, Saugman did not encounter a single case of this description, and all recent text-books on tuberculosis fail to disclose a description of or reference to a case of this kind. Very recently, however, Als[2] reported a case, stating that it was the only one so far reported in medical literature. Fishberg[3] described the second case, the first one in the English language.

In this connection the following case may prove of interest. Here we observed an effusion with multiple fluid levels on the side treated with pneumothorax and another effusion on the untreated side.

FIG. 1.—Note extent of right pneumothorax after third inflation and clear left base

G. F., aged twenty-six years, housewife, was admitted to the sanatorium on May 5, 1919. She was in perfect health until February, 1919, when she began to cough and expectorate, and occasionally noted elevation of temperature in the afternoon hours. Loss of weight and strength soon ensued and her condition was diagnosticated as pulmonary tuberculosis. On admission, physical exploration of her chest disclosed extensive infiltration of the greater part of the right lung and the left upper lobe, together with

[2] Ein Fall von Rechtsseitigen Pneumothorax Artificialis mit Linksseitigen Pleurisy Exudat, Ztschr. f. Tuberculose, 1920, xxxi, 333.

[3] A Case of Pneumothorax Complicated by Hydropneumothorax and Pleurisy, with Effusion on the Untreated Side, Am. Rev. Tuberculosis, November, 1920.

definite evidence of cavity formation at the right upper lobe. The moisture, however, was confined to the lesion on the right. Roentgenologic examination confirmed the physical findings. On account of the fever, which ranged between 101° and 103°, cough and expectoration she was put to bed at absolute rest for six weeks. No improvement followed and her general condition grew worse daily. A pneumothorax was therefore induced on the right side on June 19, 1919. The first puncture was made at the sixth interspace midaxillary line. Excellent negative pressure oscillations were found. Inflations were subsequently given at regular intervals. Fig. 1 shows the degree of collapse of right lung after the third inflation.

FIG. 2.—Note effusion and multiple fluid levels on right and pleural effusion at left base.

There was almost a miraculous change in the patient's condition. The fever abated after the third inflation. The cough and expectoration disappeared. Her appetite improved and with it an increase in strength and weight was soon noted. Her condition continued to improve until July 25, 1919, when she began to complain of headache, pain in the chest, distressing cough and nausea. Her temperature rose to 102°, but dyspnea and cyanosis were not noticeable. Two days later signs of fluid, *i. e.*, shifting flatness and succussion, were discerned on the right side, and on exploratory puncture clear fluid was aspirated. Within ten days all the constitutional symptoms of toxemia disappeared and at the end of three weeks she was again enjoying good health and was none the worse for her experience.

On September 15, 1919, she complained of severe stabbing pain in the left lower chest posteriorly, distressing cough, headache and backache, and her temperature rose to 102° F., and two days later to 104° F. There was slight dyspnea on exertion but no cyanosis was noticeable, although the prostration was unusually marked. Physical exploration of the chest disclosed in addition to the preexisting right hydropneumothorax a pleurisy with effusion on the left side. Fig. 2 shows effusion on both sides. Within five days her temperature began to decline and general improvement was noted, and by the end of three weeks all the symptoms disappeared and the left pleural effusion was absorbed. She has been in perfect health since and is now able to take care of herself and perform a fair amount of assigned exercise without untoward results.

Comment. It is noteworthy that in all the three cases thus far recorded the artificial pneumothorax was induced on the right side and that the first effusion occurred on the side of the pneumothorax. What relation this may have to the subsequent left pleural effusion is difficult to presume, but it is interesting, nevertheless.

It would be expected that with one lung completely collapsed by a pneumothorax and the other compressed by a pleural effusion the danger of respiratory embarrassment would be immense, but, as a matter of fact, dyspnea and cyanosis were not the outstanding symptoms in our case nor in the cases referred to above. The respiration at the height of the fever and both effusions never rose above 32; nor was the heart action much interfered with, for the pulse was always of a good quality and never rose above 120, regardless of the height of the fever and bilateral effusion. For these reasons it was thought advisable not to aspirate the fluid from either side. The regular inflations of the right pleural cavity were not interrupted, but greater caution was exercised in keeping the intrapleural pressure from rising too much above zero. The absorption of the left pleural effusion had no appreciable effect on the rate of absorption of the effusion on the right. The latter effusion was absorbed but slowly, undoubtedly due to the altered condition of the pleural surface resulting from the preëxisting pneumothorax. Her prognosis was not altered by the occurrence of these effusions, and she is now able to do a few hours' work without untoward effects.

EDEMA OF THE GLOTTIS IN OBSCURE DEATHS.

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The causes of death in the international list which nearly every physician has constant need for deal with *systems involved, actual infections, poisons, external causes,* the *puerperal state, malforma-*

tions and *diseases of early infancy* and *old age*. Except for the old-age group, the respiratory system list of causes is the smallest, though probably it yields a major number in the number of deaths per year if tuberculosis, pneumonia, etc., are included. The face and neck have apparently yielded the least number of deaths if one would judge from the fine print under which "nasal fossæ, larynx, thyroid body" appear: In a fairly active autopsy service[1] in which medicolegal cases are sprinkled, the same "fine print" would be applicable.

This pathological service covers the sudden and unexpected deaths that occur in the Massachusetts State hospitals: The causes of these deaths have been analyzed in a series of 262 cases with autopsy, and a list is here appended.

ANALYSIS, AUTOPSIED CASES (SUDDEN DEATHS).

	1913 –14	1914 –15	1915 –16	1916 –17	1917 –18	1918 –19	Total.
Heart lesions	4	9	13	13	16	5	60
Acute infections,	11	13	8	4	9	7	52
Foreign bodies in larynx	3	2	7	2	2	..	16
Epilepsy	1	6	..	5	4	..	16
General paresis	3	1	2	6	1	3	16
Homicides	3	3	3	1	2	..	12
Suicides	3	3	1	3	3	5	18
Tuberculosis	1	2	2	3	2	3	13
Fractures	1	3	1	1	2	7*	15
Cerebral hemorrhages	..	..	5	..	1	..	6
Thrombosis	2	..	..	2	..	..	4
After tube feeding	1	..	1	1	..	1	4
Burns	1	1	..	..	..	1	3
Hemorrhage	1	..	1	..	2	..	4
Brain tumor	..	..	2	..	..	2	4
Asphyxia	..	1	..	1	..	..	2
Katatonic "Hirntod"	..	..	1	1	..	..	2
Acute mania	1	..	..	1	..	..	2
Collapse after bath	..	1	..	..	..	..	1
Salvarsan	..	..	..	..	..	2	2
Fall	1	..	..	..	..	0	1
Edema brain	1	..	..	..	..	0	1
Arteriosclerosis	1	..	..	..	..	1	2
Ruptured bladder	..	..	1	..	..	0	1
Carcinoma	..	..	1	..	2	1	4
Drowned (accident)	..	..	..	1	..	0	1
Pernicious anemia	..	..	..	..	1	0	1
Acute gastritis	..	..	..	..	1	0	1
Edema glottis	..	..	..	..	1	0	1
Ruptured spleen	..	..	..	..	1	0	1
Ruptured heart	..	..	..	..	1	0	1
Alcohol	..	..	..	..	..	1	1
?	..	..	..	..	..	1	1
Totals	39	45	49	45	51	33	262

[1] The Pathological Service of the Department of Mental Diseases (Massachusetts) has 200–250 autopsies annually in the State Hospitals under its control to which it seeks to supply service where their laboratory activities are suspended from vacation, leave, illness or disabilities of their pathologists.

* Fracture complicated death.

It is striking to note in this list that few deaths are due to edema of the glottis, but unless the deaths are obscure the practice of removing the neck organs is not extensive. There are objections enough to cover in obtaining permission for an autopsy and promises of restoration of cosmetic possibilities in the way of embalming are necessary; to this end the neck organs are left uncut and the data therefore are not always available or not considered regarding edema of the glottis.

The clinical varieties of edema of the glottis are eleven:

1. General anasarca.
2. Infections.
3. Tumors of thyroid or cervical region.
4. Foreign bodies.
5. Trauma.
6. Posture.
7. Neuropathic (Quincke).
8. Toxic.
9. Thermal.
10. Ischemic.
11. Irritant (gas).

If we keep these clinical varieties in mind the obscure sudden deaths may not seem so obscure. 6 to 10 might be considered elaborate, though 6 is a variety seen by medical examiners in autopsies in old alcoholics who sleep on park benches or other peaceful spots with the chin sinking on the chest. In this position they are found dead, and the medical examiner returns a cause of death as due to "edema of the glottis, postural." Variety 7 necessitates infinite care in history and autopsy observations, as do 8, 9 and 10.

The causes of edema are five:

1. Arterial congestion.
2. Stagnation of the blood.
3. Hindrance to outflow of blood.
4. Disturbance of capillary secretion due to changes in capillary walls.
5. *Ex vacuo.*

The mechanisms of edema in general, as recorded in general text-books, involve the condition of lymph channels and lymph, of the bloodvessels and the blood. If the blood is thin (as in anemia and kidney disease) it goes through the vessels more easily, and also whatever is the cause of the thinning of the blood may act unfavorably on the bloodvessel walls. Now whether stagnation of flow, or overdistention because of defective innervation of the capillaries, is present, or obstruction of lymph, the result is a transudation of the liquid elements of the blood. The effect of inflammation on the vessel walls is, of course, a degenerative one, allowing more elements to pass through them. The following

cases are presented to illustrate the deaths directly dependent on edema of the glottis, each case being definite and leaving no borderline of *wrinkling* as evidence. They are compared with a glottis upon which no suggestion of edema could be passed.

1920.42. This glottis presents slow edema due to repeated trauma in an insane white male, aged thirty-three years. The patient died within twelve hours of the first known attack, that of choking him with a towel twisted about his neck. It is probable that not a single choking would have produced this grade of edema, since it takes some hours to produce physiological edema, *e. g.*, in the parturient canal. The evidence presented in court by an eye-

FIG. 1.—Traumatic edema. Death within twelve hours.

witness was that there were applications of the towel at twenty- to thirty-minute intervals. There was no lesion in the body tending otherwise to transudation of serum. The cardiorenal-vascular system was in no wise affected. There was no infectious process in the body, no tumors in the cervical region and no foreign body in the larynx.

The picture shows the water sac edema on the surfaces of the arytenoid cartilages. In the recent state the coaptation of these swelled cartilages closed the passage for air.

The patient, 1915.66, an insane criminal, aged sixty-one years, complained of a pain in his head for seven weeks. No medication

FIG. 2.—Found dead in bed. Toxic edema from pus in pituitary.

FIG. 3.—Edema and new growth from irritation of a foreign body.

relieved it and an intense central headache that interfered with sleep and kept him drowsily awake was almost constant. No increase of temperature was recorded in these seven weeks. He was found dead in bed with edema of the glottis and pus in the pituitary and postpharyngeal tissues. Further dissection shows the pituitary to contain pus, the clinoid and sella turcica to be eroded and the sphenoidal sinuses to contain purulent material. It is thought that a posterior nasal infection was followed by a sphenoid

FIG. 4.—Moderate terminal edema in a tuberculous Chinaman. Note tubercles on inner surface of epiglottis.

involvement which later was transferred to the pituitary and sella turcica; an abscess in the gland followed and erosion of its bony envelope. Infiltration through the soft tissues of the foramen magnum and anterior cervical region to the pharynx and glottis continued where toxic edema extended to the glottis and vocal cords—and death came through increased difficulty of breathing.

This patient, 1920.78, presents a terminal edema of the glottis due to the presence of a foreign body in the larynx. The patient

was an imbecile and after the ingestion of meat had a violent choking and coughing spell which was followed two days later by diphtheria. The physicians who saw him in his period of choking could find no cause for it; examination and manipulation were unavailing and the subsequent diphtheria put them off the track, though the patient always maintained he had a bone in his throat. Periodic neck distress was relieved by gentle massage of his throat and warm applications, but one night two years after the bone was lodged he died during one of these attacks.

FIG. 5.—Glottis with no edema.

The autopsy showed a slender, irregular meat bone, not unlike a portion of a vertebra, its end embedded in the mucosa of the larynx 3 cm. below the vocal cords. There were wasp-nest-like growths at the ends of the embedded bone. The tissues over the glottis were wrinkled heavily and gray. It is thought that the growth at this stage prevented the flow of air through the rima glottis in a periodic transient edema due to the irritation of the foreign body.

This patient, 1920.108, a Chinaman, aged forty-one years, died of pulmonary tuberculosis—a process thought to be of about one year's duration. This lesion was also present in the intestines. Grossly, except for anomalies, there was little otherwise to call pathological. The kidneys, arteries and heart were free from marked changes, and the Wassermann reaction on fluid and serum were negative post mortem. There was no edema elsewhere.

Summary. Edema of the glottis is for the most part clinically a local lesion, but can be a fatal termination in general anasarca and in infections. In obscure deaths careful removal of the neck organs should not be omitted.

REVIEWS.

RATIONAL TREATMENT OF PULMONARY TUBERCULOSIS. By CHARLES SABOURIN, M.D., Medical Director of the Durtol Sanatorium, Puy-de-Dome, France. From the sixth, revised and enlarged French Edition. Pp. 440. F. A. Davis Company, Philadelphia, 1921.

THIS is a rather unique book in that it appears without a preface or introduction. The work is an English translation of the sixth French edition, but the translator's name is not mentioned. Sabourin is a well-known French phthisiotherapeutist, and gives evidence of having a large experience in this field

No especially new thoughts are presented, and many older ideas and theories are still included in this edition. The subject matter is well covered and all features of treatment are touched upon in sufficient detail. The French are supertherapeutists, and apparently the author is no exception to the rest of his countrymen. He has directed the treatment of consumptives for thirty years, and as such his discussion on creosote, lime salts, tincture of iodine, sulphurous and arsenical waters as remedial agents in pulmonary tuberculosis is exceedingly interesting. The use of guaicol rubbed into the skin as an antipyretic measure is an unusual suggestion.

The translation must be a rather close one and as such the English is at times labored. The work is comprehensive; its viewpoint is sane; two qualifications which should commend the book to all phthisiologists and others interested in pulmonary tuberculosis and its treatment.

T. G. S.

NOTES ON THE MEDICAL TREATMENT OF DISEASE FOR STUDENTS AND YOUNG PRACTITIONERS OF MEDICINE. By ROBERT DAWSON RUDOLF, C.B.E., M.D. (EDIN.), F.R.C.P., Professor of Therapeutics in the University of Toronto; Clinician, Toronto General Hospital; Consulting Physician, Victoria Hospital for Sick Children, Toronto; etc. Pp. 457; 3 diagrams. University of Toronto Press; 1921.

THIS is an eminently practical text-book on therapeutics and only such facts as have a direct bearing upon the treatment of dis-

eased individuals are included. Throughout the work it is apparent that the author is constantly thinking of patients and not merely of disease in an abstract sense. He divides the consideration of the treatment of a diseased person into five parts: diagnosis, environment, diet, removal of the cause of the ailment, and symptomatic therapy. This arrangement is strictly adhered to, and, on account of its simplicity, if for no other reason, it is believed to be valuable.

Under diagnosis he has emphasized particularly the value of a complete understanding of the patient, his habits, surrounding circumstances, resisting power, etc., not being satisfied with a mere name for a diagnosis; and yet he has avoided the temptation of including a presentation of all the possible symptoms of the various diseases. He has not forgotten that many patients have to be treated before the diagnosis is established or when it is only a probability, and warns against undue attention being given to clinical laboratory results.

Under treatment proper he takes up first the environment, discussing under this heading matters of isolation, nursing, exercise, climate, etc., and making the interesting observation that in chronic conditions, when a climate must be decided upon, it is often found that the best is that one in which the patient has spent his early life. Under the heading of diet are given concisely his personal views, and it may be noted that he believes distinctly in rather free feeding in typhoid fever. By specific treatment he refers to the removal of the cause, as when the stomach is rid of a poison, and to specific therapy. Finally symptomatic treatment is taken up, and very sane views are expressed as to the value of drugs. As a guide to the student and young practitioner this work will be found most valuable. T. G. M.

Feebleness of Growth and Congenital Dwarfism. By Murk Jansen, Lecturer on Orthopedic Surgery, University of Leyden, Holland. Pp. 82; 40 illustrations. London: Oxford Medical Publication, 1921.

It is stated in the introductory note that this monograph is an attempt to work out two principles, *viz.*; (1) Injurious agents affecting growing cell-groups enfeeble their power of growth. (2) The measure in which growth is enfeebled is proportional to the rapidity of growth.

By comparing the children of the same parents in large families the effects of injurious influences on feebleness of growth are studied. Rather convincing evidence is brought forward to support the author's claims of the causation of congenital dwarfism. It is shown how smallness of the amnion may cause local dwarfism or local death of the rapidly growing parts of the embryo by direct pressure

or by indirect hydrostatic pressure. The result on the fetus depends on the relative time the pressure is exerted. Thus pressure in the third or fourth week of intra-uterine life causes anencephaly; in the fifth or sixth week, achondroplasia; in the seventh week, Mongolian idiocy, and so on.

The book is well written, the illustrations are good and one's interest is held throughout. A. G. M.

TRANSACTIONS OF THE ASSOCIATION OF AMERICAN PHYSICIANS; Thirty-fifth Session, Atlantic City, N. J., May 4 and 5, 1920. Pp. 322; vol. xxxv. Philadelphia, 1920.

THIS volume contains the papers read at the 1920 session of the Association of American Physicians. Most of them have appeared in some medical journal or other and must be stamped as an unusually good group of presentations. "Intrathoracic Teratomata," by Lambert and Knox, is a splendidly prepared article covering its subject very completely. "Epinephrin Hypersensitiveness and its Relation to Hyperthyroidism" by Peabody *et al.*, is convincingly written on this matter concerning an endocrinopathy. Fussell and Wolferth report a rare case of slow auriculoventricular rhythm and paroxysmal tachycardia with interruptions of the fast rate. Stengel, Wolferth and Jonas show the futility of using lowered oxygen tension breathing as a test of circulatory function. Many other articles are included, too numerous to mention. This volume of the transactions appears in its usually good style and reflects further credit upon the secretary of this splendid association.

T. G. S.

A TEXT-BOOK OF PHARMACOLOGY AND MEDICAL TREATMENT FOR NURSES. By J. M. FORTESCUE-BRICKDALE, M.A., M.D. (OXON.) M.R.C.P. (LOND.), Capt. R.A.M.C. (T.F.), Physician to the Bristol Royal Infirmary and Clinical Lecturer to the University of Bristol, etc. Pp. 392; 72 illustrations and 5 colored plates. London: Henry Frowde, Hodder and Stoughton, 1920.

WHILE this text-book, with its kymographic tracings, charts showing urine, chloride, and nitrogen elimination curves, and diagrams of various nerve fiber connections, immediately strikes one as being quite pretentious for nurses, who ordinarily have little or no grounding in laboratory work, yet a careful perusal of it reveals a presentation of the subject that is simple and sufficiently elementary. The first section is devoted to the known facts in regard to the action of various drugs on the animal body, the drugs not being

arranged in a wholly scientific manner but in such a way as to be easily understood and remembered. The illustrations are in every instance apt and add much to the clarity of the presentation.

The second section deals with the treatment of the common and more important diseases. Stress is placed on the principles of treatment, and at the same time the practical methods of applying these principles is not neglected. Treatment by methods other than by the giving of drugs is accorded proper consideration.

In the three appendices are considered the various poisonings and their treatment, the methods of disinfection, and radiotherapeutics, a very satisfactory exposition of the underlying principles involved in the use of the roentgen-rays and radium being included.

This book will be of distinct value not only as a text-book for student nurses, but as a reference work for graduate nurses and physicians. T. G. M.

DERMATOLOGY. By WALTER JAMES HIGHMAN, M.D., Chairman, Section on Dermatology and Syphilology, American Medical Association, Member of the American Dermatological Association, and New York Dermatological Society; Associate Professor of Dermatology, New York Post Graduate Medical School and Hospital; formerly Instructor in Dermatology, Cornell University Medical School; Acting Associate Dermatologist, Mt. Sinai Hospital, New York; Adjunct Dermatologist, Lenox Hill Hospital, New York; Pathologist, Department of Dermatology, Vanderbilt Clinic, New York, etc. Pp. 482; 95 illustrations. New York City: The Macmillan Company, 1921.

HIGHMAN has written his book on dermatology on the basis of a correlation between internal and external conditions; in other words, that in many instances a skin eruption is an external manifestation of an internal cause, thus forming the connecting link between the old Viennese school, headed by Hebra, which viewed dermatology as virtually limited to the skin, on the one hand, and the French School which considered cutaneous outbreaks from the internist's point of view. As Highman has succinctly put it "thus, while the Germans, were cataloguing dermatoses without reasoning backwards from them, the French were studying etiology without reasoning forward."

The ideal classification of cutaneous affections is naturally from the etiologic point of view but this offers many difficulties as a careful study of this excellent work will show. According to the writer, "dermatology is not a science sui generis, but a branch of internal medicine with all that this concept implies."

As one views Highman's excellent tabulation on "skin diseases which are not autochthonous," in other words not of external causa-

tion, it seems like a dream of the future rather than a realization of the present.

We can all agree with the writer that internal conditions modify the skin's reaction to external irritants and that many of the cutaneous outbreaks have their origin from within. Unfortunately, however, in how many instances can we state positively the exact internal reason for an outbreak?

Although all of the skin affections are mentioned, the finer type used for the less important diseases is of help for the beginner in this subject or the busy practitioner in culling out those affections more frequently observed. Photographs have been selected for their help in diagnosis and their grouping together is of use in showing the differences and resemblances between diseases having the same type of cutaneous outbreak.

Highman has lived up to his convictions that the term "Eczema" is meaningless and although it is used parenthetically this class of cases is placed under dermatitis.

The preparations recommended for the treatment of the eruptions are those which have proved successful in the hands of the writer.

There are very few writers on medical subjects who are as concise, lucid and with such powers of description and it is a pleasure to peruse Highman's work. F. C. K.

INSECTS AND HUMAN WELFARE. AN ACCOUNT OF THE MORE IMPORTANT RELATIONS OF INSECTS TO THE HEALTH OF MAN, TO AGRICULTURE, AND TO FORESTRY. By CHARLES THOMAS BRUES, Assistant Professor of Economic Entomology, Bussey Institution, Harvard University. Pp. 104; 42 illustrations. Cambridge: Harvard University Press. London: Humphrey Milford, Oxford University Press, 1920.

THIS book, as stated in the preface, "is an attempt to present some of the principles and practices of economic entomology in a form that will illustrate the biological relationships of insects to their environment." One not familiar with recent progress in this field of science will be surprised at its great practical importance, not only in the relation of insects to public health, but also to the food supply and to forestry. A special chapter is devoted to household insects; houseflies, stable-flies, roaches, crickets, clothes moths, etc., receiving attention. Of all the insects it is interesting that only two are of outstanding usefulness to man, the honey-bee and the silkworm. While many are directly harmful, of others it can only be said they are nuisances.

The accomplishments of the medical profession in the reduction of malaria, yellow fever, plague, and typhus fever are due to an appreciation of the relation of insects to these diseases, and for

these discoveries medical investigators must share honors with the entomologists. One interested in these important problems will thoroughly appreciate this concise yet illuminating book.

T. G. M.

TUBERCULOSIS OF THE CHILDREN. By PROFESSOR HANS MUCH, Director of the Department for the Science of Immunity and for Research of Tuberculosis at the University of Hamburg, Germany. Pp. 156; not illustrated. New York: The Macmillan Company, 1921. Translated by Max Rothschild, M.D.

THERE are two parts to this small volume. The first section is a treatise on Much's theories of immunity and the treatment of tuberculosis by partial antigens, or, as Much calls them, "partigens." The author believes that tuberculosis always starts in the first years of childhood, and that tuberculosis in the adult develops from this childhood infection. Persons once infected are protected against subsequent infection. The principle enunciated by Much, in the treatment of tuberculosis by tuberculin, hinges on the fact that there are two kinds of oversensitiveness, a harmful one (toxin) and a useful one (antibody). In the tuberculins on the market substances are present which can produce oversensitiveness to toxin as well as to antibodies. It is the separation of these substances and the administration of the proper partial antigen which gives the good results.

In Part II the necessity for the fight against tuberculosis in children is stressed. Tuberculosis of the bronchial glands is discussed at length, as in the majority of cases these glands represent the first site of invasion and localization for the bacilli.

Besides specific treatment, other methods are mentioned and their use noted. Such, for example, are roentgen-rays, salt baths, calcium, nutrition, rest, climate and artificial sunlight.

There is much of interest between the covers of this book. The theory of the "partigens" is unique as far as the reviewer is able to ascertain, and if substantiated the method of specific treatment will be revolutionary.

A. G. M.

VOLUMES II AND III OXFORD SYSTEM OF MEDICINE, Oxford University Press; 35 West 32d Street, New York.

IT would indeed be difficult to justly review the contents of these two volumes in lines many times the number allotted for this purpose, Volume II contains twenty chapters with 817 pages, while Volume III has fifteen chapters with 828 pages devoted to a wide variety of topics included in the field of internal medicine. These

chapters have a distinguished authorship and present their subject-matter with a certain degree of present-day finality. Usually a lone reviewer is liable to regard some system contributions as stronger than others, some as weaker, dependent somewhat upon his own interests. Such a reviewer will, however, find that the chapters in these two Oxford System Volumes are quite uniformly well done and highly satisfactory. Of necessity, they cannot all possess equal merit.

In Volume II, one of the most interesting chapters is devoted to the "Respiratory Excursion of the Thorax." This gives Hoover an opportunity to epitomize his ideas concerning the clinical observation of costal margin movements and the normal antagonism of the diaphragm and intercostal muscles. "Bronchial Asthma and Hay Fever" are well taken care of by Walker. These allied conditions are entertainingly discussed and much space is devoted to protein sensitivity in relation to these diseases. The details of specific protein therapy are reviewed in clear, hopeful detail. What must be considered the masterpiece chapter of this volume is Cecil Drinker's contribution on "The Pathological Physiology of Blood Cell Formation and Blood Cell Destruction." It is difficult to conceive of anything more comprehensive and thorough in execution. The bibliography of this chapter is most complete as are the bibliographies at the end of most of the chapters. Minot devotes splendid pages to the "Clinical Discussion of the Anemias." In addition to these especially interesting chapters, one finds others devoted to all diseases of the lungs, bronchi, mediastinum, heart, bloodvessels and blood.

Volume III presents an equally good lot of chapters. Each one makes its especial appeal. They are devoted to diseases of the gastro-intestinal tract, nephritis, and disturbances of the ductless glands. Perhaps the best chapters of this volume are those given to nephritis. Henry Christian, the American editor of the System, presents this subject in masterful style. The case method is utilized to good advantage, and valuable diet lists are included. Sippey covers gastroduodenal ulcer from his well known angle, while Rehfuss takes up the remaining conditions of the stomach, placing emphasis upon certain points resulting from the fractional method of investigating gastric function. Sir John Rose Bradford discusses war nephritis with no new ideas on the subject. The other English contributor to the volume, Sir Humphrey Rolleston, gives one an excellent analysis of conditions pertaining to the liver, gall-bladder and bile ducts. Pratt handles the diseases of the pancreas in his usually excellent style, while Stockton takes up the intestinal derangements. Pincoffs and Boggs deal with the peritoneum. Riesman and Horax write of adrenal and pituitary dysfunction respectively. Plummer's chapter on the thyroid and parathyroid, although planned for this volume, will be included in a later issue.

These volumes maintain the high standard set by the first one. Their chapters present the best medicine we know today, and much is omitted that has been erroneously included in text-books for years. It is interesting to note generally the concise statement of therapeutic suggestions. The supertherapeutist will look in vain for long lists of superlatively useless remedies to be tried on his patients. A very excellent feature, incorporated in these volumes, is the table of contents at the head of each chapter. This enables the reader to see at a glance what he may expect and where he may find it. These volumes have not been read in their entirety, still enough has been covered to enable one to highly commend the authors and heartily recommend their lines to those interested in internal medicine and its practice. T. G. S.

PROGRESS

OF

MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

W. S. THAYER, M.D.,

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ROGER S. MORRIS, M.D.,

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AND

THOMAS ORDWAY, M.D.,

DEAN OF UNION UNIVERSITY (MEDICAL DEPARTMENT), ALBANY, N. Y.

Dislocation of the Navel in Gastric Ulcer and Other Abdominal Affections.—H. SCHLESINGER (*Wiener klin. Wschr.*, 1921, xxxiv, 1) describes a new sign in connection with gastric ulcer and other acute lesions in the abdomen. If one has the patient sit and strain as if at stool, one frequently notices a characteristic dislocation of the navel. With healthy persons the navel is usually elevated. With an acute abdominal lesion, causing unilateral rigidity of the rectus abdominis, a lateral dislocation of the navel occurs during straining, which lasts several seconds. This transitory dislocation of the navel is toward the diseased side, because of the more marked muscular contraction. The phenomenon is best appreciated if the observer stands at the foot of the bed. The dislocation varies much in different cases (up to 4 cm.). The author finds the navel phenomenon of value at times as evidence that an ulcer persists when other signs, such as tenderness on pressure, have disappeared. Oppenheim has described dislocation of the navel as a sign of unilateral paralysis of the abdominal muscles. Here, the navel is dislocated toward the normal side. Schlesinger has observed his navel phenomenon especially in cases of gastric and duodenal ulcer and in cholelithiasis during or immediately after an attack.

Koranyi's Phenomenon.—H. FASCHINGBAUER and H. NOTHNAGEL (*Wiener klin. Wschr.*, 1921, xxxiv, 46) report their observations on Koranyi's phenomenon. In 1918, Koranyi recommended percussion of the apices of the lungs in the erect posture and with the patient leaning forward. "If the apices are sound, the percussion findings remain

the same in both postures, whereas the upper borders of diseased apices move forward if one marks their position in relation to the spinal column. Thus, asymmetries are recognizable which are missed in the erect posture. Dull areas move, their extent increases. Occasionally small areas of dulness become evident, which are missed in the usual method of carrying out percussion of the apices." The authors confirm Koranyi's findings and are convinced of the practical importance in the diagnosis of beginning apical tuberculosis. In addition to infiltrative lesions of the apices, they have found analogous phenomena in pulmonary emphysema.

Are there Reliable Criteria of Operability in Exophthalmic Goiter.—CHEEVER, D. (*Arch. Surg.*, 1921, ii, 21). From a review of the literature on the subject and an analysis of 4 fatal operative cases at the Peter Bent Brigham Hospital and 6 other cases in which a fatal issue was narrowly averted, the author concludes: (1) During an acute exacerbation of the disease or in periods of great mental depression, operation is contraindicated. (2) Muscular weakness so great that the patient cannot walk, and marked loss of weight with continued loss under absolute rest, are serious contraindications. (3) Organic visceral disease, so serious as to jeopardize patients having an operation of similar technical type, is a contraindication. (4) Operation should not be undertaken in the presence of an enlarged thymus, until its probable activity has been reduced by irradiation. (5) The Jewish race offers a distinctly higher operative mortality. (6) A metabolism of + 30 introduces a serious risk, which undoubtedly increases with high rates, but not necessarily in proportion, and there is no rate of metabolism which alone contraindicates minor surgical procedures. (7) The "vagotonic" type is possibly more vulnerable to the operative ordeal than is the "sympatheticotonic," but evidence on this point is as yet inconclusive. (8) The minor procedures, whether consisting of injections into the gland, cauterizing, or ligating operations, are often most valuable indices of a patient's resistance to trauma.

Advantages of Prophylactic Administration of Quinine Demonstrated Experimentally.—ETIENNE and EDMOND SERGENT (*Ann. de l'Institut Pasteur*, 1921, xxxv, 125). Remarking that a better way of judging the value of quinine prophylaxis against malaria is that of properly controlled experimentation, rather than simple observation, and pointing out the impossibility of this procedure when man is used as the subject, the authors worked with malaria of birds (Plasmodium relictum). The research included (1) a study of the acute infection, (2) the passage from acute to chronic states (3) the curative action of quinine and (4) the preventive action of quinine. Their general conclusions are as follows: (1) If a healthy subject (canary) absorbs quinine as a prophylactic measure, and receives a heavy inoculation of the virus, it will not become sick. On the other hand, the control birds always become ill, 30 per cent. of them dying in the acute stage. (2) This immunity following quinine persists as long as the virus is administered. Where this treatment is stopped the birds are susceptible to infection. (3) The advantages of prophylactic administration of quinine are: (*a*) avoidance of the serious accidents of the acute disease; (*b*) if the

infection is not completely avoided it is rendered much less severe, and confers on the subject a relative immunity to reinoculations; (*c*) subjects when given quinine as a prophylactic measure are less dangerous as a source of virus for inoculation of others.

Studies in the Treatment of Malaria.—STEPHENS, YORK ET AL. (*Ann. Trop. Med. and Parasit.*, 1921, xiv, 365). In a study of the time of onset of the paroxysms in simple tertian malaria it was found that 90 per cent. of the paroxysms, in cases observed occurred during the hours of activity (7 A.M. to 6.59 P.M.). The maximum number of these paroxysms occurred at 2 P.M. Alteration of the period of activity by one hour produced a corresponding alteration in the time of incidence of the paroxysms.

Variations in the Bacterial Flora of the Upper Air Passages during the Course of Common Colds.—BLOOMFIELD, A. (*Johns Hopkins Hosp. Bull.*, 1921, xxxii, 121). From facts obtained from careful review of the literature on the subject of colds, and from a consideration of the clinical features of the condition, Bloomfield summarizes our present knowledge of the subject as follows: "(1) The common cold is a definite disease generically related to grippe and influenza. The primary disease is often followed by local complications which tend to overshadow the picture. (2) Cold may produce disturbances in the upper air passages which are not to be distinguished from true infectious colds. (3) None of the common bacteria found in the nose or throat have been proved to be the primary cause of colds. (4) The most convincing evidence in the literature favors a filtrable virus as the cause of the common cold."

To investigate the subject further the author made an intensive study of the aërobic flora of the upper air passages of ten individuals suffering from acute coryza, previous studies on normal flora serving as a background. It was found that in uncomplicated colds the flora differed in no fundamental way from the normal. Where an organism normally not present was found, it almost invariably was found in cases presenting complications (bronchitis, tonsillitis, sinusitis, etc.). While it is certain that commonly encountered pathogenic bacteria, such as Staphylococci, Streptococci, Pneumococci, B. influenzæ, etc., are not etiological factors in colds, it seems that the latter may so alter the mucous membrane as to encourage its bacterial invasion by one of these organisms, resulting in the complications commonly met with following coryza.

Variations of Acid Concentrations in Different Portions of the Gastric Chyme, and its Relation to Clinical Methods of Gastric Analysis.—GORHAM, F. (*Arch. Int. Med.*, 1921, xxvii, 434). Feeling that the gastric chyme is not, in the majority of instances, a homogeneous mixture after a test meal, and that the acidity of different portions of it may vary widely, the author introduces the following method of examination: The fasting stomach is emptied and the patient given 30 gm. of dry shredded wheat biscuit and 400 c.c. of water. After forty-five minutes the entire stomach contents are aspirated in 10 c.c. portions in rapid succession. The acidity of these different portions is

determined separately and, by examining a mixture of all samples, the "average acidity" is ascertained. This method is advocated as being superior to the so-called "fractional method," where only a small sample is withdrawn, which may not be representative of the contents remaining in the stomach. The author feels that the "secretory variations" revealed by the "fractional" method of gastric analysis may be explained in part by the fact that the acidity of the fractions removed represents only the acidity of the chyme at the moment of removal in those parts of the stomach from which they were obtained as above.

Paroxysmal Tachycardia of Ventricular Origin, and its Relation to Coronary Occlusion.—ROBINSON, G. C., and HERRMAN, G. R. (*Heart*, 1921, viii, 59). On reviewing 16 reported cases of paroxysmal tachycardia of ventricular origin in which electrocardiograms are published these authors find only 6 undoubted cases. Six others are classified as probable cases of ventricular paroxysmal tachycardia. To this first group (undoubted cases) they add 4 of their own cases. Attention is called to the proved relationship between ventricular paroxysmal tachycardia and coronary occlusion in experimental animals. In one of the 4 human cases herein reported direct evidence of the association of ventricular paroxysmal tachycardia with coronary occlusion was obtained at autopsy. It is felt (for reasons cited) that this relationship was probably present in the remaining 3 cases. The prognosis of paroxysmal tachycardia of ventricular origin is more unfavorable (3 of the 4 cases dying) than that of auricular origin.

Jaundice after Salvarsan.—BROCQ, L. (*Bull. médical, Paris*, 1921, xxxv, 235). The author notes that jaundice following intravenous neoarsphenamine treatment indicates injury to liver cells, which, if not subjected to further damage, soon recover. However, these damaged cells offer a *locus minoris resistentiæ* for spirochetes, so that a complete suspension of treatment seems contraindicated. He suggests, in such a dilemma, the use of mercury or of neoarsphenamine subcutaneously, and insists that in either case the procedure must be carried out with the greatest caution.

SURGERY

UNDER THE CHARGE OF

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Pericardiotomy for Suppurative Pericarditis.—POOL (*Ann. of Surg.*, 1921, lxxiii, 393) says that two features have become generally accepted, first approach and drainage should be to the left of the sternum, secondly

no procedure should be employed which does not drain the lowest part of the pericardium. He offers an improved method—resection of portions of seventh, sixth and fifth cartilages, wherein the pericardium is opened at its lowest point; little risk to the pleura is involved, while ample drainage is provided. Moreover, whatever exploration is necessary either at the time of operation or postoperatively is provided for the added fourth interspace is exceedingly wide. Resection of the sixth and the seventh cartilages seems best in cases where less extensive exposure is imperative. Indeed, this procedure was used in the author's case, giving satisfactory exposure and efficient drainage. The drain was removed in thirty-six hours in the reported case with the substitution of two Carrel tubes and Dakin's solution was introduced regularly. In another case Carrel-Dakin method would be instituted immediately. From former experience and study of case reports, it was felt that thick pus with fibrin would likely wall off the cavity into chambers with resulting retained excretions and subsequent imperfect drainage, especially of the left recess. In theory, it was believed that the solvent effect of Dakin's solution would obviate this risk by rendering the excretions thin. Improvement was striking and sustained, while there was no noxious influence exerted upon the pericardium apparently. Early treatment with Dakin's solution may possibly diminish pericardial adhesions. Resection of sixth cartilage alone may be done readily under local anesthesia and is indeed tempting, by reason of its simplicity, but drainage is not sufficient.

Gastro-enterostomy in Acute Perforated Ulcer of Stomach and Duodenum.—DEAVER and PFEIFFER (*Ann. of Surg.*, 1921, lxxiii, 441) say that all success in perforated ulcer is based on early treatment—early operation and efficient suture of the opening are essential. In subsidiary measures excision of the ulcer offers nothing of immediate life-saving value, while primary gastro-enterostomy is still a debated issue. The senior author has performed primary gastrojejunostomy for fifteen years with very satisfactory end results in a large series of 67 cases. The chief contraindication is the presence of shock or evident systemic toxemia—not frequent within twelve hours after perforation.

Congenital Torticollis.—MEYERDING (*Jour. Orthopedic Surgery*, 1921, iii, 91) says that torticollis of congenital origin is a deformity rarely met with in the general practice of medicine and surgery. The etiologic factor appears to be trauma to the sternocleidomastoid muscle at or preceding birth, producing an ischemia with resulting chronic interstitial myositis. Heredity, infection and syphilis do not seem to be factors. The treatment is surgical as early as possible with subsequent retentive apparatus. Operative technic is outlined.

Hallux Valgus Rigidus and Malleus.—JANSEN (*Jour. Orthopedic Surgery*, 1921, iii, 87) says that two principles make themselves felt in these deformities: (1) disturbance of muscle balance—most prominent in hallux valgus and (2) joint wear, the arthritis deformans of textbooks—most prominent in hallux rigidus. This latter condition is characterized by flattening of the metatarsal head with gradual shorten-

ing of this bone and lipping of the joint cartilage with subsequent pain through the plantar area. By cramp of the flexor brevis, hallux malleus is developed. This condition strips the abductor hallucis of its power. When the adductors prevail hallux-malleo-valgus frequently evolves, noted by the callosity on the plantar side of the interjoint of the big toe. Luxation of the extensor proprius and flexor longus hallucis is needed for hallux valgus in most cases the acknowledged effect of too narrow or too pointed shoes, especially when high heels are worn with them. From the above it follows that well fitting shoes and raising of the inner border may largely contribute toward preventing the development of these conditions. Treatment should be directed both to muscle balance and joint wear. Transplantation of abductor hallucis has proved useful to the author. In quite severe cases it may be combined with shortening of the first metatarsal according to Ludloff's method or by removal of part of the metatarsal neck.

An Integral Traction-providing Splint for Vicious Fractures of the Femur.—MASLAND (*Ann. of Surg.*, 1921, lxxiii, 495) says that all the various modifications of the Thomas and Hodgen splints are equipped with pelvic rings which give a one point support to the ischium. This permits of but limited amount of pressure without pain. The author's splint utilizes all opportunities offered by the body to distribute the strain and so allow greater traction with less discomfort. The joints above and below the fracture are immobile; the individual fit of the splints insures their better retention in position. The body and the fractured part are open for inspection and the needful attention. The strain of traction is distributed in wider degree over salient parts of the body while traction can be applied in the direction and to the degree required for traction is wholly integral to the splint. The patient can move or be moved on the bed without disturbing the direction of traction or the relation of the parts. Comfort and well-being are conserved in the highest degree.

Drainage of Common Duct through Cystic Duct: Cystico-choledochostomy.—REID (*Ann. of Surg.*, 1921, lxxiii, 458) says that Halstead advocated careful and complete closure of incision into the choledochus and drainage of this duct by a tube passed well into it by way of the ductus cysticus as early as 1897. Halstead and the author have done much work upon dogs in this problem and are now doing the operation routinely in the Johns Hopkins Hospital. Their technic is described and cases cited. The procedure offers several advantages, for the incision into the common bile duct may be closed completely and with union by first intention, while emaciation and weakness due to loss of bile for protracted periods is avoided. Healing of the abdominal wound and drainage tract is less likely to be delayed, because leakage of bile is avoided. The patency of the duct may be tested routinely by clamping the tube. Finally on removal of the tube there has been no leakage in more than one-half the cases.

A Perineal Operation for Removal of Stone in Lower End of the Male Ureter.—LOWSLEY (*Surg., Gynec. and Obst.*, 1921, xxxii, 300) says that a careful review of the anatomy of the male pelvis with careful dissection on the cadaver impressed upon him the accessibility of the lower

end of the ureter by means of the perineal route. He describes the developed technic for removal of stone by this route. The perineal route should only be attempted when the stone is less than 4 cm. from the bladder and fixed in position. The patient may be allowed out of bed after the second day and the downhill drainage would seem to be a decided advantage in that the chances of thick scar formation around the ureter are less. Moreover, this downhill drainage prevents absorption of urine and deleterious results from concomitant infection which frequently accompanies urinary lithiasis. Finally chances of wide infection of tissues around incision in ureter and subsequent stricture of ureter are much less.

Resection of Intestine for Acute Intussusception: Two Cases of Recovery.—SOUTHAM and CRAWSHAW (*British Med. Jour.*, February 19, 1921, p. 266) say that the published results show that the mortality of enterectomy in cases of acute intussusception is extremely high. In an earlier collection of 239 cases by Gibson, there was no recovery from irreducible intussusception in a patient under seven years. Barker says that he had never seen a recovery after resection in a gangrenous state and never expected to see it. The 2 reported cases were three years and six months old respectively. In both cases the intestine was gangrenous. Extensive resection was necessary but complete and uneventful recoveries followed. The successful issue was due to measures taken to safeguard the patient from the effects of shock. *Speed* in operating is essential. Everything should be ready to hand while closure of the laparotomy should be carried out by through-and-through sutures. *Body heat* should be preserved by bandaging the child in a suit of gamgee and the theater maintained as warm as possible. The anesthetic appears closely related to the amount of shock present. This was minimized by using gas and oxygen in 1 case while no anesthetic was used in the other. Shock further depends upon water starvation, resulting from the previous vomiting and loss of fluid. In both the reported cases, postanesthetic vomiting was entirely absent. Fluids were given and retained immediately after the completion of the operations.

On the End-results of Colectomies for Intestinal Stasis.—SHEEN (*British Med. Jour.*, December 22, 1921, p. 116) reports the end results of 4 complete colectomies performed in 1913–14. One of them died soon after operation. In the other three there was great improvement; in two, what might be termed complete success. The qualifying details are: in the first case a ventral hernia with dyspeptic symptoms; in the second, adhesions fortunately not interfering with pregnancy; in the third diarrhea occasionally. There is an operative parietal infection in these and similar cases which it is justifiable to regard as coming from within. Possibly the poorly vitalized parietes cannot deal with organisms which the peritoneal cavity can put up with, in these toxic subjects. The usual germ is B. coli. In spite of the good results in these 3 cases, the author confesses that he is not enamoured of this operation. He accepts the toxemia, its signs and symptoms—that it is due to a blocking of the ileal effluent owing to displacements, kinks and adhesions of cecum and colon, these again resulting from upright posture, habitual constipation and tight clothing in women. The surgical "purists" say that there are only two lines of treatment, paraffin

and truss belts for slighter cases and colectomy for the rest. Complete colectomy is a serious operation. Very few are done, for it is not a popular operation among surgeons. The mortality is not easily ascertained. Many cases recover and are greatly benefited while some cases die. There is a third class in which there is neither death nor recovery but an almost hopeless discomfort. Clark records "final results" in 12 cases: in 6 of these it was not satisfactory. The author searches for alternatives for abdominal operations, for various kinds are done and toxemia previously present disappears. It has been said of these types of operations that their good results have been produced by freeing the ileal effluent. Waugh attributes the impairment of mechanical efficiency of the bowel to the elongated retained mesentery of the ascending colon, a developmental survival present in 20 per cent. of individuals born. An easy, safe operation—fixation of anterior colon, cures and symptoms of stasis disappear. The author has carried this operation out in several cases with immediate improvement. Surgery is not the only remedy advocated. Diets, paraffin, massage, exercises, posture, spa treatment, removal of toxic foci, all have their place in treatment of intestinal stasis. Prevention should be our final goal. It should be instituted in babyhood and continue for the earlier the treatment the better, because then the less severe and more effective it is.

Acidosis in Operative Surgery.—FARRAR (*Surg., Gynec. and Obstet.*, 1921, xxxii, 328) says that there is great need for collaboration between the surgeon and the physiologist, as the time may be all too short for the study of a condition suddenly confronting the surgeon at or immediately following an operation. Acidosis is a term used to signify an impoverishment of the body in bases. The alkali reserve (bicarbonates of the blood) is the criterion of the acid-base balance of the body. The determination of the alkali reserve is readily made by Van Slyke's method. (The number of cubic centimeters of carbon dioxide gas which 100 c.c. of blood plasma will take up.) A high carbon dioxide combining power of the blood is of the greatest importance for the maintenance of lung ventilation during operation. The range of the carbon dioxide combining power of the blood in women (150 cases) is 55.2 c.c. to 69.9 c.c. per 100 c. c. of the blood plasma or about 8 points lower than Van Slyke found for men. It follows, therefore, that acidosis is more frequent following operations in women than in men. The fall in alkali reserve during operation depends not only upon the anesthetic and the duration of the operation but upon the nature of the operation and the occurrence of hemorrhage and shock. Moreover, the fall in alkali reserve bears a close relation to the fall in blood-pressure and pulse pressure. If a fall in blood-pressure is prevented, there is a saving in alkali reserve. A solution of glucose given intravenously during an operation at the rate of 0.8 gram of glucose for every kilogram of body weight each hour of the operation will lessen the acidosis incident to operation by promoting metabolism. Vomiting is diminished and diuresis promoted by this measure. Glucose will appear in the urine in one-half hour if this rate has been exceeded. A solution of gum acacia (6 per cent.) in a glucose solution (20 per cent.), if given a subtolerant rate the entire time of operation, is an aid to the maintenance of blood-pressure.

PEDIATRICS

UNDER THE CHARGE OF
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A Mild Chronic Nephritis in Children.—HILL (*Jour. Am. Med. Assn.*, August 28, 1920) gives the test that he uses to determine the presence of acute nephritis. In mild cases a fixation is shown where the phenolsulphonephthalein test is normal. A fixation does not necessarily mean a severely damaged kidney, but it is an indication at least that the kidney function is abnormal. The child is put on a full normal diet containing a considerable amount of protein, especially at the noon meal. A capsule containing 1 gm. of salt and a 2 grain pill of caffein sodium benzoate is given with each meal, to take the place of the tea or coffee used in the adult test diet. This gives a diet containing a considerable amount of salt, protein and diuretic material, all of which will stimulate the kidney to its maximum effort. Exactly 10 ounces of fluid is given with each meal and no fluid or food whatever is given between meals. The urine is collected in two-hour periods from 7 A.M. to 7 P.M. and the night urine from 7 P.M. to 7 A.M. Then all that is required is to record the specific gravity of each sample of urine. The normal response shows a wide variation in gravity between the different specimens; in fifteen normal children there was always a variation of at least eight points between the highest and the lowest. The night urine in normal children is small in amount, and almost always has a specific gravity of 1020 or over. The child with damaged kidneys on the other hand, is unable to vary the concentration of the urine in this way, and the gravity of the individual specimens may vary only one or two points. The fixation may be at a high or at a low level, and may be high or low in the same patient at different times. It is apparently the fixation of the gravity that is important and not the level at which it is fixed. This is the most practical test for everyday use. There is nothing complicated about it. The food does not have to be weighed, nor is it necessary for the patient to eat all of it. It is merely essential that he consume a good full diet. The rules for fluid intake must, however, be strictly adhered to. As regards blood urea, the writer thinks that the fixation is shown even in cases where there is not sufficient damage to give marked urea retention.

Weight and Height in Relation to Malnutrition.—EMERSON and MANNY (*Arch. Ped.*, August, 1920) point out that malnutrition is a definite clinical entity with characteristic history, definite symptoms and pathological physical signs. Clinical evidence shows that the physical signs that may best serve to identity this group of malnourished children is the relationship between weight and height. The age factor is of secondary importance, and is mainly serviceable in selecting cases stunted by constitutional disabilities such as syphilis, tuberculosis, deficient thyroids, the effect of certain drugs, convalescence from long

illness and the like. The tables derived from the studies of Boas and Burk represent the most extensive records of weights and heights made. Recent studies show that they are essentially true averages for unselected groups of American children. The Boas-Burk and other tables in general use are vitiated by the measurements of large numbers of malnourished children, whose measurements lower the averages of weight and height, and make them of only relative value as standards. By setting the Boas-Burk figures the depression of averages is to a great part offset. Individual variations in the relationship of weight to height is of enough importance to make it necessary to use a zone system rather than any single line as a basis of reference. After various experiments at determining zone boundaries, clinical evidence is best satisfied by lines lying between 7 per cent. below and 20 per cent. above the "set-forward Boas-Burk figures." Outside of the central zone are found, on the one hand, the obese, and on the other, the malnourished. Within the zone are still a considerable number of malnourished children requiring individual diagnosis. The malnourished child selected by this rule of habitual 7 per cent. underweight for height form almost without variation 20 to 40 per cent. of any group of children in school and preschool periods. When tables have been constituted from sufficient numbers of children proved to be normal, the line of average weights and heights will lie somewhere between the set-forward Boas-Burke figures and those represented by a line drawn midway between the 7 per cent. underweight and the 20 per cent. overweight boundaries. This has already been confirmed by the special studies of Baldwin and Robertson.

The Circulatory Reaction to Graduated Exercise in Normal Children.—Wilson (*Am. Jour. Dis. Children*, September, 1920) gives the technic for making this study, which consisted of more than five hundred test exercises comprising one hundred and fifty complete experiments. The test exercises consisted of swinging one or two iron dumb-bells (3, 4, 5, 7 and 10 pounds each) from the floor to the full stretch of the arms overhead and back again between the legs, at a constant rate of two seconds for each swing. This was repeated from ten to sixty times to increase the amount of work. Each child performed at one visit three or four of these exercises graded from moderate to severe, until the maximum effort was approached as evidenced by marked breathlessness, flushed face, perspiration and fatigue. This was corroborated by an additional exercise of slightly increased intensity. The possible influence of one exercise upon another was eliminated by allowing a full rest between each exercise, and by varying the order of exercises on subsequent visits. The pulse rate at the wrist was taken by an assistant before each exercise until it remained constant. It was taken immediately after exercise for fifteen seconds and again at the end of one hundred and ten seconds after exercise for twenty seconds. From these counts the rate per minute immediately after exercise and at the end of two minutes were calculated. A pulse rate within six beats of preexercise rate was considered normal. If the pulse was not normal at the end of two minutes, it was taken at one-half minute intervals for from three to five minutes. The systolic blood-pressure after exercise was taken at five- and ten second intervals. Before exercise the systolic

blood-pressure was read until a constant level was reached and at frequent intervals for two minutes. From these experiments upon the circulatory reactions after exercise, it was found that the circulatory reactions to graduated exercise on normal children are similar to those in the adult. The circulatory reactions immediately following similar graduated exercises of two day intervals over a period of weeks were as a rule constant. The time required for the pulse rate to return to normal does not give much information as to the exercise tolerance of the child. A type of systolic blood-pressure after exercise showing an increased rise, delayed rise and summit, and a prolonged fall, and associated with symptoms of marked dyspnea and fatigue would seem to indicate that the exercise tolerance of the particular child has been reached or exceeded.

A Dental Clinic for Children in a Settlement.—GUTHRIE (*Jour. Am. Med. Assn.*, November 6, 1920) offers a report based on the case records of more than 8000 children, ranging in age from infancy to the sixteenth year. The records showed the age, sex, race, nutrition and history of previous infections. The school history was also noted. Record was made in every case of the number of deciduous and permanent teeth, together with the presence of cavities, abscesses or sinuses, and their location. Special dyscrasias, if present, were noted, as well as abnormal frenum, fifth cusp, and geographic tongue. Roentgen findings and Wassermann reports were recorded when made. It was found that there was a marked reduction in the number of cases of infectious diseases in the children who belonged to this clinic. There was not an epidemic in this neighborhood since the work was instituted. Two special groups of children were studied. One consisted of those who were known to be tuberculous, and the other of those who were proved cases of syphilitic infection. These were observed in order to determine the value of thorough dental care in these types of cases. In the tuberculosis group 95 per cent. of the deciduous teeth had to be removed before the eighth year on account of abscesses. In the syphilitic group only 40 per cent. had to be removed. More cases of retarded absorption of the deciduous roots were noted in the syphilitic group than in the tuberculous. In 9 cases of 60 at the thirteenth year roentgenograms were made to determine the condition of the deciduous roots. These disclosed a beginning absorption. In these 9 cases the 10 deciduous teeth were extracted first on the right side and after about six weeks the ten deciduous teeth on the left side were removed. In a few months the permanent teeth were erupted in correct position. Ulcerative stomatitis occurred with greater frequency among the children from the parochial schools. These patients were all isolated in the hospital and treated with bactericidal measures against anaërobic organisms. There were no deaths but several cases of marked deformity ensued as a result of the extensive operative procedure necessary to overcome the infection.

Meningitis Caused by Lead Poisoning in a Child of Nineteen Months.—STRONG (*Arch. Ped.*, September, 1920) reports this case which was admitted to the hospital for a persistent vomiting and a mild diarrhea and a temperature of 99°. The history was that about ten days pre-

viously he had been seen to bite paint from the side of his bed. After a short while he began to vomit his food. He was given castor oil by his parents and after a few days was very much better. The day before admission the vomiting and diarrhea began again. Previous to admission the child had been healthy and teething, and growth and development had been normal. The mother said that he had had a fall from bed a week before admission, and there was a small contusion over the left eye, which had disappeared for the most part and there was nothing else present to indicate that the fall had caused any serious injury. On physical examination it was found that the tonsils were hypertrophied. The vomiting was persistent. The stools of which there were four or five a day, were green in color, and contained much curds and mucus. The temperature for the first ten days after admission did not exceed at any time 100°. During the first forty-eight hours all food was withheld. The stomach was washed and the colon was irrigated. A cathartic was given. The vomiting was persistent for about a week, and at the time was considered as more than the vomiting which ordinarily accompanies an intestinal disturbance of this kind. The paint was considered as an etiological factor, but at this time no other symptoms but the vomiting could be discovered that warranted a diagnosis of lead poisoning. At the end of ten days the child had improved greatly. Because the mother was in the hospital the patient was kept in the hospital, although under ordinary circumstances he would have been discharged. During the following week the improvement was marked. One morning the nurse discovered him biting on the painted rail of his bed, and it was seen that he had bitten off some of the paint, his stomach was washed and he was given a cathartic. The bed was draped with sheets so that he could not get to the painted part. For twenty-four hours he did not give any evidence of any ill-effect from taking the paint this second time. At the end of this time he vomited his food, and the persistent vomiting and diarrhea returned. These symptoms continued for a week and it seemed to be the logical belief that the lead was the cause of the trouble. On or about the eighth day stippled red cells, Grawitz's granules, were shown. About the same time a blue line was observed on his gums near the upper incisors. On the tenth day after the recrudescence of the vomiting, distinct meningeal symptoms appeared. The head was retracted, and the extremities were extended and rigid. Kernig's sign was negative. Brudzinski's neck sign was positive. Brudzinski's collateral reflex was negative. The child seemed distinctly toxic. A ptosis of the left upper lid was occasionally present. The child was comatose most of the time. There was variable pupillary reflex, and occasional strabismus of the left eye inward. There was no nystagmus. The respiration was markedly irregular as to time and depth and later became of the Cheyne-Stokes type. The temperature did not rise to above 100° until just before death, when it rose rapidly to 103°. Laboratory examinations were for the most part negative except for the Grawitz's granules in the blood and the findings of a serous meningitis in three spinal fluids. Convulsions were few and milder than were expected. The child died on the twelfth day after the appearance of the meningeal symptoms. The etiological diagnosis was based on the presence of Grawitz's granules,

the lead line and the history of twice having ingested paint from his bed. The recognized fact that lead is capable of affecting the central nervous system, and the absence of any infection seem to justify the conclusion that the meningitis was due to lead poisoning.

The Treatment of Pyelitis in Infancy and Childhood.—KRETSCHMER and HELMHOLTZ (*Jour. Am. Med. Assn.*, November 13, 1920) treated a series of 11 cases by pelvic lavage with silver nitrate. They claim nothing new for the treatment by pelvic lavage, and they do not think that silver nitrate is a specific. The excellent results obtained in the treatment of B. coli infections in adults by means of silver nitrate injections of the renal pelvis seem to justify an attempt to treat a series of cases by this method in order to determine whether or not this could be applied to the treatment of pyelitis in infants and children, and whether this method was a better one than the treatment by medicines and vaccines. There are two factors that have prevented this method from being employed more frequently and these are because it is not generally known that it is possible and because general anesthesia is necessary. With the rapid advance in developing and perfecting small cystoscopes, this field has been materially enlarged so that cystoscopy can be performed in infants as easily as in adults. In boys, because of anatomic considerations, cystoscopy cannot be carried out as early as in girls, but one of the authors has done this repeatedly in boy babies of fourteen months. It has been suggested that external urethrotomy be done in boys to facilitate the procedure, but this has not been done. The youngest patient was seven months of age. In this case both ureters were catherized simultaneously, and both renal pelves were treated with silver nitrate. The oldest child was ten and a half years. The other patients were one child one and a half years; one two years old; two two and a half years old; one five years; one seven years; two eight and a half years. All these cases were girls. No untoward symptoms followed instrumentation and treatment. The object sought was to render the urine free from pus and sterile. No case was considered cured until these were accomplished. In 9 of the 11 cases complete cures were obtained. The cultures were reported sterile if no growths were found at the end of forty-eight hours. In order not to overlook the possibility of the development of slow growing organisms, the plates were kept in the incubator for five days before a final report of a sterile culture was given, so that in all of the cases it can be said that the culture was negative after five days. One patient left after one treatment, and the cultures showed the presence of infection. This is not included under the cured cases, although the urine was free from pus. Silver nitrate solution was used in each case. The strength of the solution was 0.5 per cent. The amount injected varied from 1 c.c. in the infants to 5 c.c. in the older children. The number of injections required to render the urine sterile varied. Three patients required but one injection. Five required two injections and one required three injections. In 2 cases the kidney urines were sterile before the bladder urines, in 1 case after two injections and in 1 case after one injection. This patient had a B. paratyphosus infection. A subsequent examination after one week showed that the kidneys were again infected. In 10 of the 11

cases the colon bacillus was found in pure culture. The eleventh case was the one just mentioned. In all the cases the pyelitis was bilateral. In none of them was a colon cystitis found; that is, in which the bladder infection alone was present. Routine leukocyte counts were made on all urines. This method gives a more accurate estimation of the amount of pus present in the urine. Further in comparing the counts it can be readily seen how the improvement is progressing.

OBSTETRICS

UNDER THE CHARGE OF

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The Prevention and Treatment of Puerperal Sepsis. — BONNEY (*British Med. Jour.*, August 21, 1920) contributes the first paper in a discussion upon the subject, before the British Medical Society. In considering the original source of the organisms which infect a puerperal patient, he differs from the view commonly held that infection is introduced from without. He holds that infection in some cases originates from intrinsic sources, although he recognizes that this is not the view which up to now has been generally held. He believes that infection from extrinsic sources caused the epidemics of puerperal sepsis which formerly decimated obstetric hospitals. These have been largely abolished by the introduction of antisepsis and where a series of cases occur in the practice of a midwife or doctor, such must be ascribed to an extrinsic source. At the present time, however, he believes that puerperal septic infection is sporadic and not epidemic. At present the average practice of obstetrics is sufficiently clean to prevent, under ordinary circumstances, infection and when patients are not brought together in institutions such infection rarely arises. The streptococcus of high virulence is a delicate organism which dies rapidly in the open air and which is easily overgrown in an incubator by other organisms even at the temperature of the body and still more readily at the temperature of a room. If the effort is made to transplant it by experiment, it is difficult to do so, and this is probably also true regarding accidental inoculation of puerperal fever. In institutions the sterilization of instruments and appliances and the use of gloves render its occurrence unlikely and infection is less apt to occur in cases conducted in the homes of patients. In spite of these facts there is no essential diminution in the occurrence of puerperal sepsis. He estimates for every one woman who dies of sepsis, four are more or less seriously ill and besides this there are a much larger number of cases of slight fever due to minor degrees of sepsis. These facts would seem to point to the conclusion that the conveyance of septic organisms from one patient to another is comparatively rare but that there is some other medium far more common

by which infection arises. He finds that from the lower bowel and the skin about the anus, organisms capable of producing puerperal sepsis, can constantly be isolated. The extensive study of infected gunshot wounds during the recent war, shows that the more virulent bacteria in these wounds came from excrement either from the feces of the wounded person or from the feces of some other, or of some animal in the form of manure. Among these the Bacillus coli communis is that most often found. There is a streptococcus constantly present in the bowel which may cause appendicitis, pelvic inflammation, suppuration after operation in the abdomen, and puerperal or post-abortional sepsis. When the uterus is examined in puerperal sepsis the streptococcus found is not, as a rule, of this variety, but on the other hand another variety of streptococcus can be isolated from the bowel. In the large intestines the character of the organisms is constantly changing; streptococci may constantly be discharged into the cecum. A catarrhal patch on the mucous membrane of the colon, or a chronically inflamed hemorrhoid may cause a most violent puerperal sepsis. It may readily be shown that the skin about the anus and perineum contains more bacteria than any other region of the body; against this, however, it is sometimes stated that the anatomy of the human body has been the same since the human race began and yet puerperal septic infection has not always existed, and further that when the perineum was torn these lacerations frequently became contaminated with feces and yet healing by first intention may take place. While bacteria may be frequent in this region, the tissues have increased power of resistance at this point to these germs. In the removal of the appendix the very best results are obtained where every precaution is taken to prevent infection from the stump. When the rectum is resected in abdominal operations every care is taken to exclude organisms in the bowel from the operation area, and penetrating wounds of the rectum are usually followed by severe infection. When infection occurs after Cesarean section upon an infected uterus, the phenomena are the same which are observed when infection from intestinal organisms has taken place. It is very difficult in conducting labor to prevent contamination of the genital tract from the rectum. The introduction of antiseptics belonging to the aniline and chlorine group places at our disposal means for rendering tissues about the vagina practically sterile: a 1 per cent. solution of equal parts of crystal violet and brilliant green in half and half alcohol and water, may be applied to the vagina and the tissues about it may be used as a lubricant for vaginal examinations. A few use a 2 per cent. solution of iodine but ordinarily a weak solution of lysol or bichloride of mercury is employed. The latter he does not believe of any practical value. When labor is conducted with the patient upon the side the danger of infection he considers greater than when patient lies upon the back. Regarding the method by which the organisms enter the uterus he calls attention to experiments that show that there is a current from below upward in the pelvic tissues and in the uterus. It does seem possible that organisms passing through the wall of the bowel into the abdominal cavity cause puerperal sepsis. Contrary to the commonly held opinion, the writer contends that puerperal sepsis is not associated with retention of gross fragments of placental

tissue in the uterus. In a great majority of cases he believes that the uterus is completely empty after labor or abortion, hence it is of little value to explore the recently emptied uterus for the organisms are in the uterine wall almost from the beginning of the infection and have now passed more deeply in or beyond it. Infection usually spreads along the ovarian veins accompanied by lymphangitis producing thickening of the broad and other pelvic ligaments which can often be detected by palpation. When chills occur large veins are usually involved, although pyosalpinx is not common after labor at term; ovarian abscess is more frequently found, active peritonitis is unusual and is generally seen around a suppurating ovary or tube, but in fatal cases passive peritoneal infection is usually present. A blood-stained fluid rich in streptococci is present in the peritoneum in these patients. Pneumonia, pleurisy and pericarditis may also develop. In the treatment of these cases flavaine or one of the antiseptics of the chlorine group, thoroughly applied in the uterine cavity may be useful. By the time symptoms have developed in most cases the organisms are in the uterine wall beyond the reach of antiseptics, hence the practice of giving an intra-uterine douche when there is considerable fever, to wash out or destroy organisms in the uterus, is useless. If tubes be introduced by the Carrel method with the hope of destroying bacteria the process is a difficult one. The writer believes that if the uterus can be thoroughly curetted so soon as the first symptoms arise, and this be followed by insertion of irrigating tubes in the Carrel-Dakin method, this treatment may prove efficient. To be successful this should be done within twelve hours of the first considerable rise of temperature. If a considerable mass of placenta be retained, this should be removed. In treating war wounds the excision of infected tissue in the wound before infection had time to develop was often successful but in the treatment of puerperal septic infection such a method would require the performance of hysterectomy. The writer has little confidence in vaccines or the intravenous injections of antitoxic serums or antiseptic injections of colloidal metals. Ligature of the ovarian veins and lymphatics accompanied by excision frequently gives good results. The writer is accustomed in dealing with sepsis after abortion when definite thickening can be felt, to remove the whole of the thickened pelvic ligament from the side of the uterus up to the highest accessible point in the line of the ovarian vessels. He has seen marked improvement follow this procedure. Prevention, however, is far more successful than the attempt at radical cure.

The Surgical Treatment of Puerperal Sepsis.—WHITEHOUSE (*British Med. Jour.*, August 21, 1920) continues the discussion of this subject before the British Medical Association. He has applied the Carrel method to 15 cases of very severe septic infection with one death. Under anesthesia the uterus is very carefully curetted with a sharp curette; should hemorrhage follow this must be controlled before the Carrel tubes are introduced and often a gauze pack is required. The application of absolute alcohol is efficient in some cases when bleeding is severe. From four to six tubes are introduced at varying heights within the uterine cavity, these should be suffi-

ciently long so that the connecting transverse glass tube may be rested upon the pubis to permit further manipulation; the tubes can be kept in position by packing the vagina lightly with strips of bismuth or plain gauze. An antiseptic ointment is thoroughly applied to the vulva or perineum to prevent excoriation. A pad of gauze and absorbent wool is placed over the vulva and the transverse glass tube attached to the bandage over the abdomen. Fresh solution is injected every two hours. As a rule the patient's temperature falls within twelve hours and the tubes are often expelled by uterine contraction. Should the tubes be expelled while the temperature is still high, they must be replaced and for this anesthesia is usually not necessary. A well-known argument against curetting was that it broke down the zone of resistance, but it has been shown that this zone or tissue acts as a nidus for the production of bacteria. A constant application of the antiseptic solution to the interior of the uterus is essential for the success of this method. The writer's experience shows that the risk of pyemia, thrombosis or parametritis is not increased by the use of a sharp curette. When these conditions developed after treatment streptococci had already been found in the blood. The only case of parametric abscess observed by the writer developed in a patient in whom curetting was not done. This treatment cannot be carried out by any but experienced and trained obstetricians and in such cases the risk of perforation is not great. The writer has not had success by using colargol and bichloride of mercury intravenously. A solution of flavaine 1 to 1000, in normal salt, he has employed intravenously in doses of 10 to 15 c.c. given in the median basilic vein, the same technic is employed which is used in the treatment of syphilis by salvarsan. One injection is given daily, sometimes two, night and morning. The results have been good, but sufficient experience has not accumulated to justify a positive conclusion.

Intravenous Protein Therapy in Puerperal Septicemia. — Gow (*British Med. Jour.*, August 21, 1920) contributed a paper before the British Medical Association describing his experience by this method. He uses a solution of peptone injecting intravenously from 8 to 10 c.c., this is increased 2 c.c. every other day or so until from 16 to 20 c.c. are given at one time. The injection must be administered slowly and carefully. A marked and rapid fall in blood-pressure follows, the pulse becomes more frequent and if leukocytosis has been present there develops a high degree of peripheral leukopenia, this condition lasts but a short time. The quality of the pulse is of special value and the radial pulse should be counted during the injection, if more than thirty-four beats to a quarter of a minute are noted the injection is temporarily stopped. A hypodermic of adrenalin 1 to 1000 may become necessary. With the latter injections there is slight fulness in the head, slight cough, a stabbing pain in the bottom of the back or a little nausea, sometimes a chill, after the chill improvement is the rule. This treatment the writer considers a valuable adjunct to the use of sensitized vaccines. A vaccine made from the Streptococcus pyogenes may be used subcutaneously in doses of from 1 to 5,000,000, on three successive days; intravenously, larger doses may be employed. If intravenous injections are used they should not be given after eating, but when the stomach is empty if possible.

Serums and Vaccines in the Treatment of Puerperal Sepsis. — MURRAY (*British Med. Jour.*) continues the discussion of puerperal sepsis in this paper. He believes that puerperal pyelitis is not an uncommon condition but one which is frequently overlooked. If this received adequate attention many cases of sepsis readily subside. Peritoneal infection may also accompany puerperal sepsis. In these cases serums and vaccines are of very little use and if anything can be done, surgical help is required. In making a diagnosis it must be remembered that a blood culture from which no growth is obtained does not necessarily signify a sterile blood stream. If anti-streptococcus serum is given, 50 c.c. diluted with an equal amount of normal salt solution may be given intravenously. This should be repeated in from twelve to twenty-four hours unless marked improvement occurs. Fresh normal horse serum may often be added to advantage. Autogenous vaccines are also of considerable value in this condition, small doses with serum give the best results. When symptoms develop during the second week with chills, autogenous vaccines obtained by puncturing the vein during a chill, are exceedingly useful. A preparation of immunized serum from the blood of a relative or person having suitable blood and its injection into the patient, seem to be worthy of trial. The writer has had no experience in the inoculation in vaccination form of organisms devitalized but not absolutely killed. In the discussion which followed, in the Women's Hospital of Birmingham, 889 cases of puerperal sepsis, 164 died. Various methods including the Carrel, were employed without marked success. Rectal examination in place of vaginal were recommended by some. Routh, in suspicious cases is accustomed to douche the uterine cavity immediately after labor with strong iodine solution. If the temperature rises on the next day under anesthesia, the uterus should be explored by the finger, pieces of placenta or membrane removed and the interior thoroughly swabbed with gauze. From 1 to 4 per cent. solution of iodine should then be applied especially over the placental site. Fixation of the uterus or parametritic thickening was considered a favorable symptom. Chloride of iron in large doses is useful.

The Diastase-content of the Urine in the Toxemias of Pregnancy. — WALLAS (*British Med. Jour.*, August 21, 1920) has examined the blood of women in normal pregnancy finding the diastase content 10 to 33.3 units. The blood urea is normal and so is blood sugar. The urea concentration tests show 2 per cent. or more. The test indicates that normal pregnant women are in a state of unstable equilibrium as regards carbohydrate metabolism and that acetone bodies are readily produced and make their appearance in the urine. In the toxemia of pregnancy there is a large quantity of diastase in the urine. The blood analysis shows urea and sugar content normal. When vomiting of pregnancy is neurotic, the diastase in the urine is normal. In neurotic vomiting ammonia coefficient is often higher than in cases of true toxemia. When the pregnant woman has nephritis, the urine shows albumin with very low globulin. Sugar and diastase are usually below normal 10 units. The blood analysis shows the urea-content higher than normal, and marked rises occur in severe cases in which the urea content of over 0.1 gm. per cent. should be regarded as unfavorable, and uremia with fatal termination may result.

Pendulous Abdomen Complicating Rachitic Pelvis.—Micholoti (*Zentralbl. f. Gynäkol.*, May 15, 1920) describes the case of a primipara, aged forty-two years, at term, who had rupture of the membranes and forty-eight hours ineffectual labor. The abdomen was very pendulous and the uterus was sharply anteflexed, the fundus over the thigh. There were deformities in the spine, both legs, and signs of rachitis in various parts of the body. The fetus was alive. The os permitted examination by two fingers only and the lower segment was found tightly drawn over the fetal head. Under anesthesia the uterus could not be raised nor could the patient assume various postures, accordingly she was delivered by section, a large vigorous child being born. Under deep anesthesia the uterus could be raised because the muscles, previously in state of marked contraction, became relaxed.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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Studies on Measles. II. Symptomatology and Pathology in Monkeys Experimentally Infected.—In a second communication, Blake and Trask (*Jour. Exper. Med.*, 1921, xxxiii, 413) detailed the symptoms, course of the reaction and the histology of the lesions of the skin, labial mucous membrane and tongue which were found in the monkeys after intratracheal inoculations with nasopharyngeal secretions of human patients in the prëeruptive and early eruptive stages of measles. The incubation period of the sixteen monkeys inoculated on the respiratory mucous membrane was seven days in the majority of animals but varied from six to ten days. After intravenous inoculation of whole blood, the incubation period was four days. The onset was characterized by listlessness, loss of appetite, drowsiness and diminution in the total leukocyte count. At times a sharp rise in temperature was encountered. The conjunctivæ became injected, photophobia and increased lacrimation ensued and small, discrete, hyperemic macules appeared on the labial mucous membrane, which latter tended, in two or three days, to increase in number and coalesce to form a diffuse, hyperemic enanthem on the labial and buccal mucous membranes. From one to five days after onset a red, maculopapular rash appeared on the skin, as a rule coming out first on the face and eventually spreading to the neck, arm and chest, abdomen and thighs and reaching its height in two or three days, at a time where the enanthem was fading. The exanthem in turn progressively faded and by six to ten days after onset all symptoms had disappeared. Some of the enanthematous

macules showed the minute bluish, white center as seen in Koplik spots. Occasionally a moderate diarrhea was noted in the earlier stages of the reaction. No symptoms of rhinitis and bronchitis were encountered. The skin and lesions, as shown by microscopic examination after fixation in Zenker's fluid and staining with alum hematoxylin and eosin, corresponded very closely to those described in cases of human measles by Ewing and by Mallory and Medlar. The lesions of the skin occurred both in the corium and epidermis, those in the latter being less numerous and conspicuous than in the former, where they were definite and typical. In the corium, they consisted of swelling and proliferation of the endothelial cells lining the capillaries and smaller veins, accumulation of endothelial leukocytes about the capillaries and active multiplication of these emigrated leukocytes. In addition there is a moderate exudation of serum into the pericapillary tissues, where in the earlier lesions, a very few eosinophils, polymorphonuclear leukocytes and lymphocytes might be present. No diapedesis of erythrocytes could be made out. The endothelial cells of the capillary walls appeared swollen and their cytoplasm was finely granular. Occasionally one was seen in mitosis. The emigrated endothelial leukocytes were young and active. Their nuclei were frequently lobulated and in the early cases these leukocytes were in active mitosis. In the epidermis in early cases, there were minute foci of serous exudate leading to swelling and vacuolation of the epithelial cells of the Malpighian layer. The serum sometimes accumulated under the cornified layer, producing tiny vesicles. There was a slight infiltration of these foci with endothelial leukocytes. The lesions in the labial mucous membrane were essentially the same as those occurring in the skin. Invasion of the epithelium was more marked than in the case of the epidermis. The lesions in the mucous membrane of the tongue were identical with those in the labial mucosa.

HYGIENE AND PUBLIC HEALTH

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Acute Respiratory Infection in Man Following Inoculations with Virulent Bacillus Influenzæ.—CECIL and STEFFEN (*Jour. Infect. Dis.*, 1921, xxviii, 201) state that virulent influenza bacilli, when injected into the nose and throat of healthy volunteers, may excite in them an acute respiratory disease similar in many respects to influenza but falling short of the typical clinical picture. In such cases influenza bacilli, biologically identical with those inoculated, may be recovered

from the discharges as long as symptoms persist and often for some time thereafter. Filtrates of Bacillus influenzæ cultures when similarly injected into two healthy volunteers produced neither local nor constitutional reaction. The inoculation of healthy volunteers with virulent hemolytic streptococci may in some cases induce an acute follicular tonsillitis with fever and leukocytosis. A virulent pneumococcus Type IV, on the other hand, was injected into the nose and throat of two healthy volunteers with impunity.

Botulism in Cattle.—GRAHAM and SCHWARZE (*Jour. Bacteriol.*, 1921, vi, 69) isolated an anaërobic bacillus biologically resembling Bacillus botulinus (Type B) from a corn silage. Several cattle of the herd consuming the silage developed symptoms of forage poisoning on two different occasions and four animals died. It is possible that botulinus toxin in the ensilage was primarily related to the disease in question. The silage was regarded as unsafe for cattle, and after discontinuing its use in the daily rations the animals remained healthy. Botulinus antitoxin (Type B) proved efficacious in protecting guinea-pigs against lethal doses of toxin in unfiltered broth cultures produced by the anaërobic bacillus isolated from the corn silage. Forty-three cattle were injected with botulinus antitoxin and subsequently fed on silage. The animals remained apparently healthy. One control or untreated animal did not show visible illness and the value of the antitoxin in the feeding operations is therefore not conclusive. It is worthy of record that the treatment did not injure the animals and encouragement is offered for more extensive field trials in determining the value of the antitoxin in cattle against the ill-effects of otherwise nourishing rations containing Bacillus botulinus toxin which heretofore has advisedly been discarded. The latter item is of importance considering the increased cost of producing grain and forage.

Concerning the Antiseptic Action of Some Aromatic Fumes.—MACHT and KUNKEL (*Proc. Soc. for Exp. Biol. and Med.*, 1920, xviii, 68) state that while their experiments were of a crude character the results obtained were of so uniform a nature that they are inclined to conclude that the fumes produced by the burning or destructive dry distillation of various gums, spices and other aromatic substances of a similar nature certainly tend to exert an antiseptic action on the bacteria studied. This is, of course, of interest not only from the scientific point of view, but also to the historian as offering a possible explanation for the extensive employment of incense in connection with sacrificial rites, etc.

The Distribution of the Spores of Bacillus Botulinus in Nature.—MEYER and GEIGER (*Public Health Reports*, 1921, xxxvi, 4) regard the soil as the common source of the spores of the botulinus organism and cite examples to support this view. They consider it likely that the soil may be contaminated by manure. They regard the soil infection as prevailing in certain localities. The practical point is that food should be so sterilized in canning as to obviate danger. Cooking the canned food just before using is an added safeguard, and any canned fruits or vegetables showing the least sign of spoilage should be discarded.

Studies of the Nasopharyngeal Secretions from Influenza Patients.—Olitsky and Gates in recent studies (*Jour. Am. Med. Assn.*, 1921, lxxvi, 640; *Jour. Exp. Med.*, 1921, xxxiii, 373) report the cultivation, from the filtered nasopharyngeal washings from early cases of uncomplicated epidemic influenza and from the lung tissues of experimental animals, minute bodies of characteristic morphology which are strictly anaërobic, are filtrable and withstand glycerolation for a period of months. The effects on the blood and in the lungs of rabbits and guinea-pigs injected with these bodies are similar to those produced by the filtered and unfiltered nasopharyngeal secretions from early cases of epidemic influenza. The authors found that the intratracheal injection of the influenzal agent in rabbits exerts an influence on the pulmonary structures of these animals of a nature to encourage the invasion of the lung and the subsequent multiplication there, with lethal outcome, of such bacteria as the pneumococcus, streptococcus and Bacillus pfeifferi, which otherwise in the doses employed are without marked effect. The control experiments show that the injection of normal rabbit lung exerts no such predisposing influence. While the experiments are perhaps not an exact reproduction of the conditions occurring in man in secondary pneumonia following influenza they bear directly on these conditions. Concurrent infections may be regarded as of accidental nature and are not casually related to the typical effects induced in rabbits by a material wholly free from ordinary bacteria. The influenzal agent exerts an effect on the pulmonary tissue which encourages the invasion of the lung and subsequent multiplication there of ordinary bacteria, such as the pneumococcus, streptococcus and Bacillus pfeifferi. A similarity is believed to exist between the conditions under which concurrent infections arose in the inoculated rabbits and those which seem to favor the occurrence of concurrent infections during epidemic influenza in man. In no instance did death occur in the rabbits as a result of the uncomplicated effects of the influenzal agent alone. When death occurred in any of the inoculated animals concurrent infection of the lungs by ordinary bacteria was present. The microörganisms most commonly met with under these conditions were Pneumococcus Type IV and atypical Type II streptococci and hemoglobinophilic bacilli. Other kinds were encountered less often.

An Outbreak of Botulism at St. Anthony's Hospital, Oakland, Calif., in October, 1920.—Geiger (*Public Health Reports*, 1920, xxxv, 2858) reports a series of six cases of botulism due to spoiled commercial canned spinach. There were three deaths among the four severe cases. One of the cases appears to have been saved by the botulinus antitoxin. The epidemiological evidence was complete in incriminating the spinach.

Concerning Anaphylaxis Following the Administration of Diphtheria Antitoxin.—Bronfenbrenner and Schlesinger (*Proc. Soc. for Exp. Biol. and Med.*, 1921, xviii, 147) studied experimentally the question of the apparent tolerance of human beings to anaphylaxis during diphtheria intoxication. They state that sensitized guinea-pigs receiving subcutaneously large excess of diphtheria toxin withstand the intravenous injection of at least five lethal doses of the antigen to which

they were previously sensitized. This apparent resistance appears about twelve to fourteen hours after the administration of toxin and just about the time when the outward symptoms of intoxication begin to manifest themselves. With a view to eliciting the mechanism of this phenomenon they have made the following observations: The antitryptic titer of the blood of guinea-pigs injected with the toxin does not appreciably deviate from normal up to the time of death. The mechanism regulating the antitryptic titer of the blood remains unimpaired in these animals, however, since an injection of antigen to which they are sensitized is followed by a typical rise of antitrypsin. This rise of antitrypsin incidentally can be interpreted as an indication that the humoral phase of the anaphylactic response of the animals is not abolished by the previous injection of toxin. If the same dose of toxin is overneutralized with antitoxin *in vitro* before injection it does not protect the sensitized guinea-pigs from immediate death when even a single minimal lethal dose of antigen is introduced intravenously. On the contrary the same dose of toxin heated for thirty minutes at 80° C. protected guinea-pigs from anaphylactic shock just as unheated toxin did. Heating of the toxin for thirty minutes at 100° C., however, destroys this property of toxin even if a much larger amount of such toxin is injected. Since the culture medium containing toxin contains also 1 per cent. peptone, a control sensitized guinea-pig, instead of toxin, received peptone in the amount ten times that present in culture medium carrying the toxin. This guinea-pig died immediately after the intravenous injection of antigen, thus showing no protection. It seems thus that the clinical observation concerning apparent diminution of anaphylactic reactivity during diphtheria intoxication is borne out by this preliminary experiment.

Studies in the Physiology of Vitamines: Is Water-Soluble Vitamine Identical with Secretin?—COWGILL (*Proc. Soc. Exp. for Biol. and Med.*, 1921, xviii, 148) states that a similarity in the physiological effects of vitamine B and substances which promote secretion has been alleged by VOEGTLIN and MYERS (*Jour. Pharm. Exper. Therap.*, 1919, xiii, 301). The author has examined a number of solutions such as extracts of rice polish, wheat embryo, navy bean and yeast and neutralized tomato-juice, demonstrated to contain vitamine B, for their possible action on the secretory function of the pancreas and liver. The products used were tested for vitamine B content on polyneuritic pigeons and on dogs which had lost their appetite for several days after having been fed on a diet lacking this dietary essential. Vitamine B has been shown to restore appetite in such animals. The effect of the products on the flow of pancreatic juice and bile was noted in anesthetized dogs in which the pylorus was ligated to prevent secretion due to discharge of acid chyme from the stomach, and the gall-bladder bile was prevented from discharging by ligation of the cystic duct. Normal dogs and dogs fed a diet lacking vitamine B were used. It is planned to experiment upon polyneuritic dogs as well. Fresh secretin solutions prepared by the usual method were injected as a control. Except in the case of tomato-juice all of these products gave negative results. The secretin solutions, however, in comparatively small amounts always produced a characteristic and vigorous flow.

The Effect of Heat and Age Upon the Antiscorbutic Vitamine in Tomatoes.—GIVENS and MCCLUGAGE (*Proc. Soc. for Exp. Biol. and Med.*, 1921, xviii, 148) conducted feeding experiments upon guinea-pigs in order to determine the effect of heat and age upon the antiscorbutic accessory in tomatoes. They found guinea-pigs protected against scurvy by daily doses of 2.5 grams of fresh raw tomatoes; by 10 grams of fresh raw tomatoes heated one hour at 100° C.; by 2 grams of dried tomatoes heated fifteen minutes at 100° C.; by 10 grams of tomatoes canned at fifteen pounds' pressure for thirty minutes; by 3 c.c. of commercial canned tomatoes three years old, and by 10 grams commercial canned tomatoes, three years old, cooked fifteen minutes at 100° C.

Immunological Distinctions of Encephalitis and Poliomyelitis.—AMOSS (*Jour. Exp. Med.*, 1921, xxxiii, 187) states that lethargic encephalitis is an epidemic disease, the main manifestations of which relate to injury inflicted upon the central nervous system and in particular the basal ganglia of the brain. Poliomyelitis is an epidemic disease, the main manifestations of which relate to injury inflicted upon the central nervous system and in particular the gray matter of the spinal cord and medulla oblongata. At the outset of the epidemic of lethargic encephalitis the two diseases tend to prevail at distinct and different seasons of the year, although recently cases of epidemic encephalitis have arisen in the midsummer months. The two maladies therefore are perhaps less distinguished by seasonal prevalence than has been supposed. They are, however, distinguished by great differences in communicability to monkeys. Epidemic poliomyelitis is readily transmitted through inoculation of the affected central nervous tissues of man to monkeys, while it may still be regarded as doubtful whether lethargic encephalitis has been communicated to monkeys in this manner. The two diseases can be distinguished through the power of the blood serum under certain circumstances to neutralize the virus of poliomyelitis. The blood serum of convalescent cases of poliomyelitis, whether in man or monkey, possesses this neutralizing power, while the blood serum of recently convalescent cases of epidemic encephalitis is devoid of it. On the basis of the distinguishing characters described it is regarded as desirable at the present time to hold epidemic poliomyelitis and epidemic encephalitis as integrally distinct affections. The latter also may be infectious, yet the main lesions of poliomyelitis are present in the spinal cord and of epidemic encephalitis in the midbrain.

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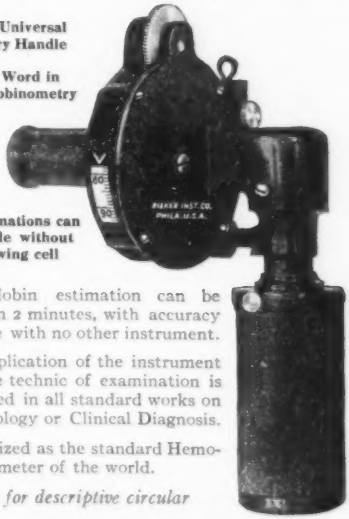

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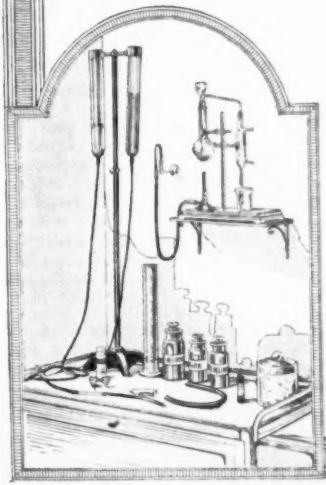

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